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	M PTO-1390 U.	S. DEPARTMENT OF	ATTORNEY'S DOCKET						
COMMERCE PATENT AND TRADEMARK OFFICE			NUMBER						
(REV	V. 1094)	L0461/7078							
	TRANSMITTAL LETTER TO THE UNITED STATES								
	DESIGNATED/ELECTED (US APPLICATION AND (IF MINING 2 CF) 29							
INTER	CONCERNING A FILING UNATIONAL APPLICATION NO.								
PCT/US98/14679 15 July 1998 (15.07.98)			PRIORITY DATE CLAIMED 17 July 1997 (17.07.97)						
TITLE OF INVENTION									
CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES APPLICANT(S) FOR DO/EO/US									
OLD, Lloyd J.; SCANLAN, Matthew J.; STOCKERT, Elisabeth; GURE, Ali; CHEN, Yao-Tseng; GOUT, Ivan; O'HARE, Michael; OBATA, Yuichi; PFREUNDSCHUH, Michael; TURECI, Ozlem; SAHIN, Ugur									
Applica	Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:								
1. X		cerning a filing under 35 U.S.C. 371.							
2.	This is a SECOND or SUBSEQUENT so	ubmission of items concerning a filing under	er 35 U.S.C. 371.						
J. 7	This express request to begin national procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).								
4. X	A proper Demand for International Prelin	ainary Examination was made by the 19th n	nonth from the earliest claimed priority date.						
5. X	- Fy and an addition of the priorition of	s filed (35 U.S.C. 371(c)(2)).							
	a. \Box is transmitted herewith (required only if not transmitted by the International Bureau)								
	 b. has been transmitted by the International Bureau. c. X is not required, as the application was filed in the United States Receiving Office (RO/US). 								
6.	A translation of the International Application into English (35 U.S.C. 371(c)(2)) with verification of translation.								
7. X	Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)). a. □ are transmitted herewith (required only if not transmitted by the International Bureau).								
	b. Li have been transmitted by the Internation	ational Bureau.	·						
	c. have not been made; however, thed. X have not been made and will not be	e time limit for making such amendments ha	as NOT expired.						
	d. A have not been made and will not be	made.							
8. 🗆	A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).								
9. 🗆	An oath or declaration of the inventor(s) (An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).							
10. 🗆	A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(C)(5)).								
Items	11. To 16. Below concern document(s)	or information included:							
11.	An Information Disclosure Statement und	er 37 CFR 1.97 and 1.98 with references.							
12. 🗆	An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.								
13. X	A FIRST preliminary amendment.								
	A SECOND or SUBSEQUENT prelimina	ry amendment.							
14. 🗆	A substitute specification (submitted as a first Preliminary Amendment).								
15. 🗆	A change of power of attorney and/or address letter.								
16. X	16. X Other items or information: Mailed via Express Mailing Label No. EL437905460US Post Card								
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Express Mail Label No. EL437905460US Dated Filed: January 14, 2000

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U.S. APPLICATION NO (1/ kno/2)	239 P 1 9	INTERNATIONAL APPLICATION		ATTORNEY'S DOCKET NUMBER					
	PC1/US98/148/9			L0461/7078 CALCULATIONS PIOUSE ONLY					
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):									
Search Report has been prepared by the EPO or JPO									
International preliminary examination fee paid to USPTO (37 CFR 1.482)									
No international probut international sea									
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO									
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) \$96.00									
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Surcharge of \$130.00 for months from the earliest	\$								
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE						
Total Claims	35-20 =	15	X \$18.00	\$270.00					
Independent Claims	19-3=	16	X \$78.00	\$1248.00					
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a. X A check in the amount of \$_2618.00 to cover the above fees is enclosed.									
b. Please charge by Deposit Account No In the amount of \$ To cover the above fees. A duplicate copy of this sheet is enclosed									
c. X The commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit									
Account No. 23/2825. A duplicate of this sheet is enclosed.									
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.									
M. Dila. a. A.									
SEND ALL CORRESPONDENCE TO SEND ALL CORRESPONDENCE TO SIGNATURE									
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WOLF, GREENFIEL	msterdam								
600 Atlantic Avenue NAME									
Boston, Massachusetts 02210 40,212									

Form)T)-1390 (REV 10-94) page 2 of 2

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ATTORNEY'S DOCKET NO. L0461/7078

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Old et al.

Serial No:

PCT/US98/14679

Filed:

July 15, 1998

For:

CANCER ASSOCIATED ANTIGENS AND USES THEREFOR

Examiner:

Not Assigned

Art Unit:

Unknown

Box PCT ASSISTANT COMMISSIONER FOR PATENTS WASHINGTON, D.C. 20231

Sir:

PRELIMINARY AMENDMENT

Please amend the application as follows.

In the Specification

Please amend the specification as follows. Please add the following paragraph as the first paragraph of the specification:

--This application is a national stage application under 35 U.S.C. §371 of PCT/US98/14679, filed July 15, 1998, which is a continuation in part of U.S. application serial no. 08/896,164, filed July 17, 1997, U.S. application serial no. 08/948,705, filed October 10, 1997, and U.S. application serial no. 09/102,322, filed June 22, 1998, all of which are now pending. This application also claims priority under 35 U.S.C. §119 to U.S. application serial no. 60/061,599, filed October 10, 1997, and U.S. application serial no. 60/061,765, filed October 10, 1997, both of which are now abandoned. This application also claims priority under 35 U.S.C. §119 to Great Britain application no. 9721697.2, filed October 11, 1997.--

In the Claims

Please delete without prejudice claims 3, 4, 6-17, 19-21, 23-30, 32-39, 41, 43, 45-48, 50-57, 60-66, 68-70, 72, 78, 80, 81, 84, 86-89, 91, 92, 94-98, 100, 101, 103, 104, 106, 107, 109-111, 113-115 and 117.

Please amend the claims as follows:

40.(amended) The composition of claim[s] 31[-38], wherein the agent is an antibody.

42.(amended) A composition of matter comprising a conjugate of the agent of claims 31[-41] and 40 and a therapeutic or diagnostic agent.

49.(amended) A pharmaceutical composition comprising
an isolated polypeptide comprising a PP Group 1 or a PP Group 2 polypeptide, <u>or an</u>
HLA binding fragment thereof and

a pharmaceutically acceptable carrier.

58.(amended) The pharmaceutical composition of claim[s] 49[-57], further comprising an adjuvant.

71.(amended) An expression vector comprising an isolated nucleic acid molecule of claim[s] 59[, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69 or 70] operably linked to a promoter.

74.(amended) A host cell transformed or transfected with an expression vector of claims 71, [72,] or 73.

75.(amended) A host cell transformed or transfected with an expression vector of claim 71 [or claim 72] and further comprising a nucleic acid encoding HLA.

76.(amended) An isolated polypeptide encoded by the isolated nucleic acid molecule of claim[s] 59[, 60, 61, 62, 63, 64, 65, or 66].

102.(amended)A method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject a pharmaceutical composition of any one of claims 18, [19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30,] 44[, 45, 46, 47, 48,] and 49[, 50, 51, 52, 53, 54, 55, 56, 47, and 58] in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

112. (amended)A composition of matter useful in stimulating an immune response to a plurality of [a] proteins encoded by nucleic acid molecules that are NA Group 1 molecules, comprising

a plurality of peptides derived from the amino acid sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

Remarks

Please enter this amendment prior to calculation of the fees. The amendments to the specification were made to correct typographical errors and reduce claims. Support for the amendment to claim 49 can be found in the claims as filed. No new matter has been added.

Respectfully submitted,

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Tel.: (617) 720-3500

Docket No.: L0461/7078 Date: January 14, 2000

X01/17/00

PCT/US98/14679

CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES

Field of the Invention

The invention relates to nucleic acids and encoded polypeptides which are cancer associated antigens expressed in patients afflicted with breast cancer. The invention also relates to agents which bind the nucleic acids or polypeptides. The nucleic acid molecules, polypeptides coded for by such molecules and peptides derived therefrom, as well as related antibodies and cytolytic T lymphocytes, are useful, *inter alia*, in diagnostic and therapeutic contexts.

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Background of the Invention

The mechanism by which T cells recognize foreign materials has been implicated in cancer. A number of cytolytic T lymphocyte (CTL) clones directed against autologous melanoma antigens, testicular antigens, and melanocyte differentiation antigens have been described. In many instances, the antigens recognized by these clones have been characterized.

The use of autologous CTLs for identifying tumor antigens requires that the target cells which express the antigens can be cultured *in vitro* and that stable lines of autologous CTL clones which recognize the antigen-expressing cells can be isolated and propagated. While this approach has worked well for melanoma antigens, other tumor types, such as epithelial cancers including breast and colon cancer, have proved refractory to the approach.

More recently another approach to the problem has been described by Sahin et al. (*Proc. Natl. Acad. Sci. USA* 92:11810-11813, 1995). According to this approach, autologous antisera are used to identify immunogenic protein antigens expressed in cancer cells by screening expression libraries constructed from tumor cell cDNA. Antigen-encoding clones so identified have been found to have elicited an high-titer humoral immune response in the patients from which the antisera were obtained. Such a high-titer IgG response implies helper T cell recognition of the detected antigen. These tumor antigens can then be screened for the presence of MHC/HLA class I and class II motifs and reactivity with CTLs

The invention is elaborated upon in the disclosure which follows.

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Summary of the Invention

Autologous antibody screening has now been applied to cancer using antisera from cancer patients. Numerous cancer associated antigens have been identified. The invention provides, *inter alia*, isolated nucleic acid molecules, expression vectors containing those molecules and host cells transfected with those molecules. The invention also provides isolated proteins and peptides, antibodies to those proteins and peptides and CTLs which recognize the proteins and peptides. Fragments including functional fragments and variants of the foregoing also are provided. Kits containing the foregoing molecules additionally are provided. The foregoing can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer associated antigens.

Prior to the present invention, only a handful of cancer associated genes had been identified in the past 20 years. The invention involves the surprising discovery of many genes, some previously known and many previously unknown, which are expressed in individuals who have cancer. These individuals all have serum antibodies against the proteins (or fragments thereof) encoded by these genes. Thus, abnormally expressed genes are recognized by the host's immune system and therefore can form a basis for diagnosis, monitoring and therapy.

The invention involves the use of a single material, a plurality of different materials and even large panels and combinations of materials. For example, a single gene, a single protein encoded by a gene, a single functional fragment thereof, a single antibody thereto, etc. can be used in methods and products of the invention. Likewise, pairs, groups and even panels of these materials can be used for diagnosis, monitoring and therapy. The pairs, groups or panels can involve 2, 3, 4, 5... to as many as 25, 50, 100 or more genes, gene products, fragments thereof or agents that recognize such materials. A plurality of such materials are not only useful in monitoring, typing, characterizing and diagnosing cells abnormally expressing such genes, but a plurality of such materials can be used therapeutically. An example of the use of a plurality of such materials for the prevention, delay of onset, amelioration, etc. of cancer cells, which express or will express such genes prophylactically or acutely. Any and all combinations of the genes, gene products, and materials which recognize the genes and gene products can be tested and identified for use according to the invention. It would be far too lengthy to recite all such combinations; those skilled in the art, particularly in view of the teaching contained herein, will readily be able to determine which combinations are most appropriate for which circumstances.

As will be clear from the following discussion, the invention has in vivo and in vitro uses,

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including for therapeutic, diagnostic, monitoring and research purposes. One aspect of the invention is the ability to fingerprint a cell expressing a number of the genes identified according to the invention. Such fingerprints will be characteristic, for example, of the stage of the cancer, the type of the cancer, or even the effect in animal models of a therapy on a cancer. Cells also can be screened to determine whether such cells abnormally express the genes identified according to the invention.

The invention, in one aspect, is a method of diagnosing a disorder characterized by expression of a cancer associated antigen precursor coded for by a nucleic acid molecule. The method involves the steps of contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an MHC, preferably an HLA, molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and determining the interaction between the agent and the nucleic acid molecule, the expression product or fragment of the expression product as a determination of the disorder.

In one embodiment the agent is selected from the group consisting of (a) a nucleic acid molecule comprising NA Group 1 nucleic acid molecules or a fragment thereof, (b) a nucleic acid molecule comprising NA Group 3 nucleic acid molecules or a fragment thereof, (c) a nucleic acid molecule comprising NA Group 17 nucleic acid molecules or a fragment thereof, (d) an antibody that binds to an expression product, or a fragment thereof, of NA group 1 nucleic acids, (e) an antibody that binds to an expression product, or a fragment thereof, of NA group 3 nucleic acids, (f) an antibody that binds to an expression product, or a fragment thereof, of NA group 17 nucleic acids, (g) and agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 1 nucleic acid, (h) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA group 3 nucleic acid, and (I) an agent that binds to a complex of an MHC, preferably HLA, molecule and a fragment of an expression product of a NA Group 17 nucleic acid.

The disorder may be characterized by expression of a plurality of cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9 or at least 10 such agents.

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In each of the above embodiments the agent may be specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.

In another aspect the invention is a method for determining regression, progression or onset of a condition characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method involves the steps of monitoring a sample, from a subject who has or is suspected of having the condition, for a parameter selected from the group consisting of (i) the protein, (ii) a peptide derived from the protein, (iii) an antibody which selectively binds the protein or peptide, and (iv) cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule, as a determination of regression, progression or onset of said condition. In one embodiment the sample is a body fluid, a body effusion or a tissue.

In another embodiment the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of (a) an antibody which selectively binds the protein of (i), or the peptide of (ii), (b) a protein or peptide which binds the antibody of (iii), and (c) a cell which presents the complex of the peptide and MHC molecule of (iv). In a preferred embodiment the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme. The sample in a preferred embodiment is assayed for the peptide.

According to another embodiment the nucleic acid molecule is one of the following: a NA Group 3 molecule, a NA Group 11 molecule, a NA Group 12 molecule, a NA Group 13 molecule, a NA Group 14 molecule, a NA Group 15 molecule, or a NA Group 16 molecule. In yet another embodiment the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.

The invention in another aspect is a pharmaceutical preparation for a human subject. The pharmaceutical preparation includes an agent which when administered to the subject enriches selectively the presence of complexes of an HLA molecule and a human cancer associated antigen, and a pharmaceutically acceptable carrier, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule which comprises a NA Group 1 molecule. In one embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

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The agent in one embodiment comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least two, at least three, at least four or at least 5 different such agents.

In another embodiment the agent is selected from the group consisting of (1) an isolated polypeptide comprising the human cancer associated antigen, or a functional variant thereof, (2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof, (3) a host cell expressing the isolated polypeptide, or functional variant thereof, and (4) isolated complexes of the polypeptide, or functional variant thereof, and an HLA molecule.

The agent may be a cell expressing an isolated polypeptide. In one embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative. In another embodiment the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell expresses an HLA molecule that binds the polypeptide. The cell can express one or both of the polypeptide and HLA molecule recombinantly. In another preferred embodiment the cell is nonproliferative. In yet another embodiment the agent is at least two, at least three, at least four or at least five different polypeptides, each representing a different human cancer associated antigen or functional variant thereof.

The agent in one embodiment is a PP Group 2 polypeptide. In other embodiments the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.

In an embodiment each of the pharmaceutical preparations described herein also includes an adjuvant.

According to another aspect the invention, a composition is provided of an isolated agent that binds selectively a PP Group 1 polypeptide. In separate embodiments the agent binds selectively to a polypeptide selected from the following: a PP Group 3 polypeptide, a PP Group 11 polypeptide, a PP Group 12 polypeptide, a PP Group 13 polypeptide, a PP Group 14 polypeptide, a PP Group 15 polypeptide, and a PP Group 16 polypeptide. In other embodiments, the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides. In each of the above described embodiments the agent may be an antibody.

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In another aspect the invention is a composition of matter .composed of a conjugate of the agent of the above-described compositions of the invention and a therapeutic or diagnostic agent. Preferably the conjugate is of the agent and a therapeutic or diagnostic that is an antineoplastic.

The invention in another aspect is a pharmaceutical composition of an isolated nucleic acid molecule selected from the group consisting of: (1) NA Group 1 molecules, and (2) NA Group 2 molecules, and a pharmaceutically acceptable carrier. In one embodiment the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule. In another embodiment the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different cancer associated antigen.

Preferably the pharmaceutical composition also includes an expression vector with a promoter operably linked to the isolated nucleic acid molecule. In another embodiment the pharmaceutical composition also includes a host cell recombinantly expressing the isolated nucleic acid molecule.

According to another aspect of the invention a pharmaceutical composition is provided. The pharmaceutical composition includes an isolated polypeptide comprising a PP Group 1 or a PP Group 2 polypeptide, and a pharmaceutically acceptable carrier. In one embodiment the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.

In another embodiment the isolated polypeptide comprises at least two different polypeptides, each comprising a different cancer associated antigen. In separate embodiments the isolated polypeptides are selected from the following: PP Group 11 polypeptides or HLA binding fragments thereof, PP Group 12 polypeptides or HLA binding fragments thereof, PP Group 13 polypeptides or HLA binding fragments thereof, PP Group 14 polypeptides or HLA binding fragments thereof, or PP Group 16 polypeptides or HLA binding fragments thereof.

In an embodiment each of the pharmaceutical compositions described herein also includes an adjuvant.

Another aspect the invention is an isolated nucleic acid molecule comprising a NA Group 3 molecule. Another aspect the invention is an isolated nucleic acid molecule comprising a NA Group 4 molecule. In separate embodiments the isolated nucleic acid molecules are selected from the following: a Group 11 molecule or a functional fragment

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thereof, a Group 12 molecule or a functional fragment thereof, a Group 13 molecule or a functional fragment thereof, a Group 14 molecule or a functional fragment thereof, a Group 15 molecule or a functional fragment thereof, or a Group 16 molecule or a functional fragment thereof.

The invention in another aspect is an isolated nucleic acid molecule selected from the group consisting of (a) a fragment of a nucleic acid selected from the group of nucleic acid molecules consisting of SEQ ID numbered below and comprising all nucleic acid sequences among SEQ ID NOs 1-816, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a human cancer associated antigen precursor, (b) complements of (a), provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of (1) sequences having the GenBank accession numbers of the sequence Group 1, (2) complements of (1), and (3) fragments of (1) and (2).

In one embodiment the sequence of contiguous nucleotides is selected from the group consisting of: (1) at least two contiguous nucleotides nonidentical to the sequence Group 1, (2) at least three contiguous nucleotides nonidentical to the sequence Group 1, (3) at least four contiguous nucleotides nonidentical to the sequence Group 1, (4) at least five contiguous nucleotides nonidentical to the sequence Group 1, (5) at least six contiguous nucleotides nonidentical to the sequence Group 1, or (6) at least seven contiguous nucleotides nonidentical to the sequence Group 1.

In another embodiment the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, 200 nucleotides, 1000 nucleotides and every integer length therebetween.

In yet another embodiment the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.

Another aspect of the invention is an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter.

According to one aspect the invention is an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule. In another aspect the invention is an expression vector comprising a NA Group 1 or Group 2 molecule

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and a nucleic acid encoding an MHC, preferably HLA, molecule.

In yet another aspect the invention is a host cell transformed or transfected with an expression vector of the invention described above.

In another aspect the invention is a host cell transformed or transfected with an expression vector comprising an isolated nucleic acid molecule of the invention described above operably linked to a promoter, or an expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 1 or 2 molecule and further comprising a nucleic acid encoding HLA.

According to another aspect of the invention an isolated polypeptide encoded by the isolated nucleic acid molecules the invention, described above, is provided. These include PP Group 1-17 polypeptides. The invention also includes a fragment of the polypeptide which is immunogenic. In one embodiment the fragment, or a portion of the fragment, binds HLA or a human antibody.

The invention includes in another aspect an isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule. In one embodiment the fragment is part of a complex with HLA. In another embodiment the fragment is between 8 and 12 amino acids in length. In another embodiment the invention includes an isolated polypeptide comprising a fragment of the polypeptide of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.

According to another aspect of the invention a kit for detecting the presence of the expression of a cancer associated antigen precursor is provided. The kit includes a pair of isolated nucleic acid molecules each of which consists essentially of a molecule selected from the group consisting of (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and (b) complements of ("a"), wherein the contiguous segments are nonoverlapping. In one embodiment the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule. Preferably, the pair amplifies a human NA Group 3 molecule.

According to another aspect of the invention a method for treating a subject with a disorder characterized by expression of a human cancer associated antigen precursor is provided. The method includes the step of administering to the subject an amount of an agent,

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which enriches selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of (a) a nucleic acid molecule comprising NA group 1 nucleic acid molecules, (b) a nucleic acid molecule comprising NA group 3 nucleic acid molecules, (c) a nucleic acid molecule comprising NA group 17 nucleic acid molecules.

In one embodiment the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen. Preferably the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

In another embodiment the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.

In yet another embodiment the disorder is cancer.

According to another aspect the invention is a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (I) removing an immunoreactive cell containing sample from the subject, (ii) contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor, (iii) introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.

In one embodiment the host cell recombinantly expresses an HLA molecule which binds the human cancer associated antigen. In another embodiment the host cell endogenously

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expresses an HLA molecule which binds the human cancer associated antigen.

The invention includes in another aspect a method for treating a subject having a condition characterized by expression of a cancer associated antigen precursor in cells of the subject. The method includes the steps of (I) identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule (ii) transfecting a host cell with a nucleic acid selected from the group consisting of (a) the nucleic acid molecule identified, (b) a fragment of the nucleic acid identified which includes a segment coding for a cancer associated antigen, (c) deletions, substitutions or additions to (a) or (b), and (d) degenerates of (a), (b), or (c); (iii) culturing said transfected host cells to express the transfected nucleic acid molecule, and; (iv) introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition. Preferably, the antigen is a human antigen and the subject is a human.

In one embodiment the method also includes the step of (a) identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule, wherein the host cell expresses the same MHC molecule as identified in (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.

In another embodiment the method also includes the step of treating the host cells to render them non-proliferative.

In yet another embodiment the immune response comprises a B-cell response or a T cell response. Preferably the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

In another embodiment the nucleic acid molecule is a NA Group 3 molecule.

Another aspect of the invention is a method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule. The method includes the step of administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.

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In one embodiment the antibody is a monoclonal antibody. Preferably the monoclonal antibody is a chimeric antibody or a humanized antibody.

In another aspect the invention is a method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method involves the step of administering to a subject at least one of the pharmaceutical compositions of the invention described above in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject. In one embodiment the condition is cancer. In another embodiment the method includes the step of first identifying that the subject expresses in a tissue abnormal amounts of the protein. The invention in another aspect is a method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the steps of (I) identifying cells from the subject which express abnormal amounts of the protein; (ii) isolating a sample of the cells; (iii) cultivating the cells, and (iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

In one embodiment the cells express a protein selected from the group consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14 protein, a PP Group 15 protein and a PP Group 16 protein. In another embodiment the method includes the step of rendering the cells non-proliferative, prior to introducing them to the subject.

In another aspect the invention is a method for treating a pathological cell condition characterized by abnormal expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule. The method includes the step of administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

In one embodiment the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody. In another embodiment the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein. In yet another important embodiment the nucleic acid molecule is a NA Group 3 nucleic acid molecule.

The invention includes in another aspect a composition of matter useful in stimulating an immune response to a plurality of a protein encoded by nucleic acid molecules that are NA Group 1 molecules. The composition is a plurality of peptides derived from the amino acid

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sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

In one embodiment at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto. In another embodiment the composition of matter includes an adjuvant. In another embodiment the adjuvant is a saponin, GM-CSF, or an interleukin.

According to another aspect the invention is an isolated antibody which selectively binds to a complex of: (I) a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and (ii) and an MHC molecule to which binds the peptide to form the complex, wherein the isolated antibody does not bind to (I) or (ii) alone.

In one embodiment the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

The invention also involves the use of the genes, gene products, fragments thereof, agents which bind thereto, and so on in the preparation of medicaments. A particular medicament is for treating cancer and a more particular medicament is for treating breast cancer, lung cancer, renal cancer, colon cancer, prostate cancer or gastric cancer.

Detailed Description of the Invention

In the above summary and in the ensuing description, lists of sequences are provided. The lists are meant to embrace each single sequence separately, two or more sequences together where they form a part of the same gene, any combination of two or more sequences which relate to different genes, including and up to the total number on the list, as if each and every combination were separately and specifically enumerated. Likewise, when mentioning fragment size, it is intended that a range embrace the smallest fragment mentioned to the full-length of the sequence (-1 so that it is a fragment), each and every fragment length intended as if specifically enumerated. Thus, if a fragment could be between 10 and 15 in length, it is explicitly meant to mean 10, 11, 12, 13, 14, or 15 in length.

The summary and the claims mention antigen precursors and antigens. As used in the summary and in the claims, a precursor is substantially the full-length protein encoded by the coding region of the isolated DNA and the antigen is a peptide which complexes with MHC, preferably HLA, and which participates in the immune response as part of that complex. Such antigens are typically 9 amino acids long, although this may vary slightly.

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As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat or rodent. In all embodiments human cancer antigens and human subjects are preferred.

The present invention in one aspect involves the cloning of cDNAs encoding human cancer associated antigen precursors using autologous antisera of subjects having cancer. The sequences of the clones representing genes identified according to the methods described herein are presented in the attached Sequence Listing, and the predicted amino acid sequences of some clones also are presented. Of the foregoing, it can be seen that some of the clones are considered completely novel as no nucleotide or amino acid homologies to coding regions were found in the databases searched. Other clones are novel but have some homology to sequences deposited in databases (mainly EST sequences). Nevertheless, the entire gene sequence was not previously known. In some cases no function was suspected and in other cases, even if a function was suspected, it was not know that the gene was associated with cancer. In all cases, it was not known or suspected that the gene encoded a cancer antigen which reacted with antibody from autologous sera. Analysis of the clone sequences by comparison to nucleic acid and protein databases determined that still other of the clones surprisingly are closely related to other previously-cloned genes. The sequences of these related genes is also presented in the Sequence Listing. The nature of the foregoing genes as encoding antigens recognized by the immune systems of cancer patients is, of course, unexpected.

The invention thus involves in one aspect cancer associated antigen polypeptides, genes encoding those polypeptides, functional modifications and variants of the foregoing, useful fragments of the foregoing, as well as diagnostics and therapeutics relating thereto.

Homologs and alleles of the cancer associated antigen nucleic acids of the invention can be identified by conventional techniques. Thus, an aspect of the invention is those nucleic acid sequences which code for cancer associated antigen precursors. Because this application contains so many sequences, the following chart is provided to identify the various groups of sequences discussed in the claims and in the summary:

"Nucleic Acid Sequences"

NA Group 1. (a) nucleic acid molecules which hybridize under stringent conditions to a molecule consisting of a nucleic acid sequence selected from the group consisting of nucleic acid sequences among SEQ ID NOs 1-816 and which code for a cancer associated antigen precursor.

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- (b) deletions, additions and substitutions which code for a respective cancer associated antigen precursor,
- (c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
 - (d) complements of (a), (b) or (c).
- NA Group 2. Fragments of NA Group 1, which codes for a polypeptide which, or a portion of which, binds an MHC molecule to form a complex recognized by a an autologous antibody or lymphocyte.
- NA Group 3. The subset of NA Group 1 where the nucleotide sequence is selected from the group consisting of:
- (a) previously unknown human nucleic acids coding for a human cancer associated antigen precursor,
- (b) deletions, additions and substitutions which code for a respective human cancer associated antigen precursor,
- (c) nucleic acid molecules that differ from the nucleic acid molecules of (a) or (b) in codon sequence due to the degeneracy of the genetic code, and
 - (d) complements of (a), (b) or (c).
- NA Group 4. Fragments of NA Group 3, which code for a polypeptide which, or a portion of which, binds to an MHC molecule to form a complex recognized by an autologous antibody or lymphocyte.
- NA Group 5. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.
 - NA Group 6. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.
- NA Group 7. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.

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NA Group 8. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.

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- NA Group 9. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.
 - NA Group 10. A subset of NA Group 1, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.
- NA Group 11. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human breast cancer associated antigen precursor.
 - NA Group 12. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human colon cancer associated antigen precursor.
 - NA Group 13. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human gastric cancer associated antigen precursor.
- NA Group 14. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human lung cancer associated antigen precursor.
 - NA Group 15. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human renal cancer associated antigen precursor.
- NA Group 16. A subset of NA Group 3, wherein the nucleic acid molecule codes for a human prostate cancer associated antigen precursor.
 - NA Group 17. A subset of NA Group 1, comprising human cancer associated antigens that react with allogenic cancer antisera.

Polypeptide Sequences

PP Group 1. Polypeptides encoded by NA Group 1.

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- PP Group 2. Polypeptides encoded by NA Group 2
- PP Group 3. Polypeptides encoded by NA Group 3.
- PP Group 4. Polypeptides encoded by NA Group 4.
- PP Group 5. Polypeptides encoded by NA Group 5.
- 5 PP Group 6. Polypeptides encoded by NA Group 6.
 - PP Group 7. Polypeptides encoded by NA Group 7.
 - PP Group 8. Polypeptides encoded by NA Group 8.
 - PP Group 9. Polypeptides encoded by NA Group 9.
 - PP Group 10. Polypeptides encoded by NA Group 10.
- 0 PP Group 11. Polypeptides encoded by NA Group 11.
 - PP Group 12. Polypeptides encoded by NA Group 12.
 - PP Group 13. Polypeptides encoded by NA Group 13.
 - PP Group 14. Polypeptides encoded by NA Group 14.
 - PP Group 15. Polypeptides encoded by NA Group 15.
 - PP Group 16. Polypeptides encoded by NA Group 16.
 - PP Group 17. Polypeptides encoded by NA Group 17.

The term "stringent conditions" as used herein refers to parameters with which the art is familiar. Nucleic acid hybridization parameters may be found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. More specifically, stringent conditions, as used herein, refers, for example, to hybridization at 65°C in hybridization buffer (3.5 x SSC, 0.02% Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% Bovine Serum Albumin, 2.5mM NaH₂PO₄(pH7), 0.5% SDS, 2mM EDTA). SSC is 0.15M sodium chloride/0.15M sodium citrate, pH7; SDS is sodium dodecyl sulphate; and EDTA is ethylenediaminetetracetic acid. After hybridization, the membrane upon which the DNA is transferred is washed, for example, in 2 x SSC at room temperature and then at 0.1 - 0.5 x SSC/0.1 x SDS at temperatures up to 68°C.

There are other conditions, reagents, and so forth which can be used, which result in a similar degree of stringency. The skilled artisan will be familiar with such conditions, and thus they are not given here. It will be understood, however, that the skilled artisan will be able to

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manipulate the conditions in a manner to permit the clear identification of homologs and alleles of cancer associated antigen nucleic acids of the invention (e.g., by using lower stringency conditions). The skilled artisan also is familiar with the methodology for screening cells and libraries for expression of such molecules which then are routinely isolated, followed by isolation of the pertinent nucleic acid molecule and sequencing.

In general homologs and alleles typically will share at least 40% nucleotide identity and/or at least 50% amino acid identity to the sequences of breast cancer associated antigen nucleic acid and polypeptides, respectively, in some instances will share at least 50% nucleotide identity and/or at least 65% amino acid identity and in still other instances will share at least 60% nucleotide identity and/or at least 75% amino acid identity. The homology can be calculated using various, publicly available software tools developed by NCBI (Bethesda, Maryland) that can be obtained through the internet (ftp:/ncbi.nlm.nih.gov/pub/). Exemplary tools include the BLAST system available at http://wwww.ncbi.nlm.nih.gov. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydropathic analysis can be obtained using the MacVetor sequence analysis software (Oxford Molecular Group). Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention.

In screening for cancer associated antigen genes, a Southern blot may be performed using the foregoing conditions, together with a radioactive probe. After washing the membrane to which the DNA is finally transferred, the membrane can be placed against X-ray film to detect the radioactive signal. In screening for the expression of cancer associated antigen nucleic acids, Northern blot hybridizations using the foregoing conditions (see also the Examples) can be performed on samples taken from breast cancer patients or subjects suspected of having a condition characterized by expression of breast cancer associated antigen genes. Amplification protocols such as polymerase chain reaction using primers which hybridize to the sequences presented also can be used for detection of the cancer associated antigen genes or expression thereof.

The breast cancer associated genes correspond to SEQ ID NOs. 1-40 and 66. The preferred breast cancer associated antigens for the methods of diagnosis disclosed herein are those set forth in SEQ ID NOs:[31, 33 and 34], which were found to react with allogeneic breast cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The colon cancer associated genes correspond to SEQ ID Nos. 544-586, even numbers

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only. The preferred colon cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic colon cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The gastric cancer associated genes correspond to SEQ ID NOs 176-436 and 588-674. The preferred gastric cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic gastric cancer antisera. Encoded polypeptides

(e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The renal cancer associated genes correspond to SEQ ID Nos. 89-169, odd numbers only, and 170, 172, and 174. The preferred renal cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic renal cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The lung cancer associated genes correspond to SEQ ID Nos. 689, 691, 692, 694, 696-707, 709, 711, and 712. The preferred lung cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic lung cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The prostate cancer associated genes correspond to SEQ ID NOs 437-543. The preferred prostate cancer associated antigens for the methods of diagnosis disclosed herein are those, which were found to react with allogeneic prostate cancer antisera. Encoded polypeptides (e.g., proteins), peptides and antisera thereto are also preferred for diagnosis.

The invention also includes degenerate nucleic acids which include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Thus, it will be apparent to one of ordinary skill in the art that any of the serine-encoding nucleotide triplets may be employed to direct the protein synthesis apparatus, in vitro or in vivo, to incorporate a serine residue into an elongating breast cancer associated antigen polypeptide. Similarly, nucleotide sequence triplets which encode other amino acid residues include, but are not limited to: CCA, CCC, CCG and CCT (proline codons); CGA, CGC, CGG, CGT, AGA and AGG (arginine codons); ACA, ACC, ACG and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus,

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the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides isolated unique fragments of cancer associated antigen nucleic acid sequences or complements thereof. A unique fragment is one that is a 'signature' for the larger nucleic acid. It, for example, is long enough to assure that its precise sequence is not found in molecules within the human genome outside of the cancer associated antigen nucleic acids defined above (and human alleles). Those of ordinary skill in the art may apply no more than routine procedures to determine if a fragment is unique within the human genome. Unique fragments, however, exclude fragments completely composed of the nucleotide sequences of any of GenBank accession numbers listed in Table 1 or other previously published sequences as of the filing date of the priority documents for sequences listed in a respective priority document or the filing date of this application for sequences listed for the first time in this application which overlap the sequences of the invention.

A fragment which is completely composed of the sequence described in the foregoing GenBank deposits is one which does not include any of the nucleotides unique to the sequences of the invention. Thus, a unique fragment must contain a nucleotide sequence other than the exact sequence of those in GenBank or fragments thereof. The difference may be an addition, deletion or substitution with respect to the GenBank sequence or it may be a sequence wholly separate from the GenBank sequence.

Unique fragments can be used as probes in Southern and Northern blot assays to identify such nucleic acids, or can be used in amplification assays such as those employing PCR. As known to those skilled in the art, large probes such as 200, 250, 300 or more nucleotides are preferred for certain uses such as Southern and Northern blots, while smaller fragments will be preferred for uses such as PCR. Unique fragments also can be used to produce fusion proteins for generating antibodies or determining binding of the polypeptide fragments, or for generating immunoassay components. Likewise, unique fragments can be employed to produce nonfused fragments of the cancer associated antigen polypeptides, useful, for example, in the preparation of antibodies, and in immunoassays. Unique fragments further can be used as antisense molecules to inhibit the expression of cancer associated antigen nucleic acids and polypeptides, particularly for therapeutic purposes as described in greater detail below.

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As will be recognized by those skilled in the art, the size of the unique fragment will depend upon its conservancy in the genetic code. Thus, some regions of cancer associated antigen sequences and complements thereof will require longer segments to be unique while others will require only short segments, typically between 12 and 32 nucleotides (e.g. 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 and 32 or more bases long, up to the entire length of the disclosed sequence. As mentioned above, this disclosure intends to embrace each and every fragment of each sequence, beginning at the first nucleotide, the second nucleotide and so on, up to 8 nucleotides short of the end, and ending anywhere from nucleotide number 8, 9, 10 and so on for each sequence, up to the very last nucleotide, (provided the sequence is unique as described above).

Virtually any segment of the polypeptide coding region of novel cancer associated antigen nucleic acids, or complements thereof, that is 18 or more nucleotides in length will be unique. Those skilled in the art are well versed in methods for selecting such sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from other sequences in the human genome of the fragment to those on known databases typically is all that is necessary, although *in vitro* confirmatory hybridization and sequencing analysis may be performed. Especially preferred include nucleic acids encoding a series of epitopes, known as "polytopes". The epitopes can be arranged in sequential or overlapping fashion (*see, e.g.*, Thomson et al., *Proc. Natl. Acad. Sci. USA* 92:5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15:1280-1284, 1997), with or without the natural flanking sequences, and can be separated by unrelated linker sequences if desired. The polytope is processed to generated individual epitopes which are recognized by the immune system for generation of immune responses.

Thus, for example, peptides derived from a polypeptide having an amino acid sequence encoded by one of the nucleic acid disclosed herein, and which are presented by MHC molecules and recognized by CTL or T helper lymphocytes, can be combined with peptides from one or more other cancer associated antigens (e.g. by preparation of hybrid nucleic acids or polypeptides) to form "polytopes". The two or more peptides (or nucleic acids encoding the peptides) can be selected from those described herein, or they can include one or more peptides of previously known cancer associated antigens. Exemplary cancer associated peptide antigens that can be administered to induce or enhance an immune response are derived from tumor associated genes and encoded proteins including MAGE-1, MAGE-2, MAGE-3, MAGE-4, MAGE-5, MAGE-6, MAGE-7,

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MAGE-8, MAGE-9, MAGE-10, MAGE-11, GAGE-1, GAGE-2, GAGE-3, GAGE-4, GAGE-5, GAGE-6, BAGE-1, RAGE-1, LB33/MUM-1, PRAME, NAG, MAGE-Xp2, MAGE-Xp3, MAGE-Xp4, tyrosinase, brain glycogen phosphorylase, Melan-A, and MAGE-C1. See, for example, PCT application publication no. WO96/10577. Other examples will be known to one of ordinary skill in the art (for example, see Coulie, *Stem Cells* 13:393-403, 1995), and can be used in the invention in a like manner as those disclosed herein. One of ordinary skill in the art can prepare polypeptides comprising one or more peptides and one or more of the foregoing cancer associated peptides, or nucleic acids encoding such polypeptides, according to standard procedures of molecular biology.

Thus polytopes are groups of two or more potentially immunogenic or immune response stimulating peptides which can be joined together in various arrangements (e.g. concatenated, overlapping). The polytope (or nucleic acid encoding the polytope) can be administered in a standard immunization protocol, e.g. to animals, to test the effectiveness of the polytope in stimulating, enhancing and/or provoking an immune response.

The peptides can be joined together directly or via the use of flanking sequences to form polytopes, and the use of polytopes as vaccines is well known in the art (see, e.g., Thomson et al., *Proc. Acad. Natl. Acad. Sci USA* 92(13):5845-5849, 1995; Gilbert et al., *Nature Biotechnol.* 15(12):1280-1284, 1997; Thomson et al., *J. Immunol.* 157(2):822-826, 1996; Tam et al., *J. Exp. Med.* 171(1):299-306, 1990).for example, Tam showed that polytopes consisting of both MHC class I and class II binding epitopes successfully generated antibody and protective immunity in a mouse model. Tam also demonstrated that polytopes comprising "strings" of epitopes are processed to yield individual epitopes which are presented by MHC molecules and recognized by CTLs. Thus polytopes containing various numbers and combinations of epitopes can be prepared and tested for recognition by CTLs and for efficacy in increasing an immune response.

It is known that tumors express a set of tumor antigens, of which only certain subsets may be expressed in the tumor of any given patient (for examples of this, see the Examples below). Polytopes can be prepared which correspond to the different combination of epitopes representing the subset of tumor rejection antigens expressed in a particular patient. Polytopes also can be prepared to reflect a broader spectrum of tumor rejection antigens known to be expressed by a tumor type. Polytopes can be introduced to a patient in need of such treatment as polypeptide structures, or via the use of nucleic acid delivery systems known in the art (see, e.g., Allsopp et al., Eur. J.

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Immunol. 26(8):1951-1959, 1996). Adenovirus, pox virus, Ty-virus like particles, adeno-associated virus, plasmids, bacteria, etc. can be used in such delivery. One can test the polytope delivery systems in mouse models to determine efficacy of the delivery system. The systems also can be tested in human clinical trials.

In instances in which a human HLA class I molecule presents tumor rejection antigens derived from cancer associated nucleic acids, the expression vector may also include a nucleic acid sequence coding for the HLA molecule that presents any particular tumor rejection antigen derived from these nucleic acids and polypeptides. Alternatively, the nucleic acid sequence coding for such a HLA molecule can be contained within a separate expression vector. In a situation where the vector contains both coding sequences, the single vector can be used to transfect a cell which does not normally express either one. Where the coding sequences for a cancer associated antigen precursor and the HLA molecule which presents it are contained on separate expression vectors, the expression vectors can be cotransfected. The cancer associated antigen precursor coding sequence may be used alone, when, e.g. the host cell already expresses a HLA molecule which presents a cancer associated antigen derived from precursor molecules. Of course, there is no limit on the particular host cell which can be used. As the vectors which contain the two coding sequences may be used in any antigen-presenting cells if desired, and the gene for cancer associated antigen precursor can be used in host cells which do not express a HLA molecule which presents a cancer associated antigen. Further, cell-free transcription systems may be used in lieu of cells.

As mentioned above, the invention embraces antisense oligonucleotides that selectively bind to a nucleic acid molecule encoding a cancer associated antigen polypeptide, to reduce the expression of cancer associated antigens. This is desirable in virtually any medical condition wherein a reduction of expression of cancer associated antigens is desirable, e.g., in the treatment of cancer. This is also useful for *in vitro* or *in vivo* testing of the effects of a reduction of expression of one or more cancer associated antigens.

As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules

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are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions. Based upon the sequences of nucleic acids encoding breast cancer associated antigen, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases which are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., Nature Biotechnol. 14:840-844, 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen which are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., Cell Mol. Neurobiol. 14(5):439-457, 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of a cancer associated antigen. Thus, the present invention also provides for antisense oligonucleotides which are complementary to the genomic DNA corresponding to nucleic acids encoding breast cancer associated antigens. Similarly, antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end

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of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art recognized methods which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness.

The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, nucleic acids encoding breast cancer associated antigen polypeptides, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term

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"pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term "physiologically acceptable" refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials which are well known in the art, as further described below.

As used herein, a "vector" may be any of a number of nucleic acids into which a desired sequence may be inserted by restriction and ligation for transport between different genetic environments or for expression in a host cell. Vectors are typically composed of DNA although RNA vectors are also available. Vectors include, but are not limited to, plasmids, phagemids and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector may be cut in a determinable fashion and into which a desired DNA sequence may be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence may occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication may occur actively during a lytic phase or passively during a lysogenic phase. An expression vector is one into which a desired DNA sequence may be inserted by restriction and ligation such that it is operably joined to regulatory sequences and may be expressed as an RNA transcript. Vectors may further contain one or more marker sequences suitable for use in the identification of cells which have or have not been transformed or transfected with the vector. Markers include, for example, genes encoding proteins which increase or decrease either resistance or sensitivity to antibiotics or other compounds, genes which encode enzymes whose activities are detectable by standard assays known in the art (e.g., ß-galactosidase or alkaline phosphatase), and genes which visibly affect the phenotype of transformed or transfected cells, hosts, colonies or plaques (e.g., green fluorescent protein). Preferred vectors are those capable of autonomous replication and expression of the structural gene products present in the DNA segments to which they are operably joined.

As used herein, a coding sequence and regulatory sequences are said to be "operably" joined

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when they are covalently linked in such a way as to place the expression or transcription of the coding sequence under the influence or control of the regulatory sequences. If it is desired that the coding sequences be translated into a functional protein, two DNA sequences are said to be operably joined if induction of a promoter in the 5' regulatory sequences results in the transcription of the coding sequence and if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region to direct the transcription of the coding sequences, or (3) interfere with the ability of the corresponding RNA transcript to be translated into a protein. Thus, a promoter region would be operably joined to a coding sequence if the promoter region were capable of effecting transcription of that DNA sequence such that the resulting transcript might be translated into the desired protein or polypeptide.

The precise nature of the regulatory sequences needed for gene expression may vary between species or cell types, but shall in general include, as necessary, 5' non-transcribed and 5' non-translated sequences involved with the initiation of transcription and translation respectively, such as a TATA box, capping sequence, CAAT sequence, and the like. Especially, such 5' non-transcribed regulatory sequences will include a promoter region which includes a promoter sequence for transcriptional control of the operably joined gene. Regulatory sequences may also include enhancer sequences or upstream activator sequences as desired. The vectors of the invention may optionally include 5' leader or signal sequences. The choice and design of an appropriate vector is within the ability and discretion of one of ordinary skill in the art.

Expression vectors containing all the necessary elements for expression are commercially available and known to those skilled in the art. See, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. Cells are genetically engineered by the introduction into the cells of heterologous DNA (RNA) encoding a breast cancer associated antigen polypeptide or fragment or variant thereof. That heterologous DNA (RNA) is placed under operable control of transcriptional elements to permit the expression of the heterologous DNA in the host cell.

Preferred systems for mRNA expression in mammalian cells are those such as pRc/CMV (available from Invitrogen, Carlsbad, CA) that contain a selectable marker such as a gene that confers G418 resistance (which facilitates the selection of stably transfected cell lines) and the

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human cytomegalovirus (CMV) enhancer-promoter sequences. Additionally, suitable for expression in primate or canine cell lines is the pCEP4 vector (Invitrogen), which contains an Epstein Barr Virus (EBV) origin of replication, facilitating the maintenance of plasmid as a multicopy extrachromosomal element. Another expression vector is the pEF-BOS plasmid containing the promoter of polypeptide Elongation Factor 1α, which stimulates efficiently transcription *in vitro*. The plasmid is described by Mishizuma and Nagata (*Nuc. Acids Res.* 18:5322, 1990), and its use in transfection experiments is disclosed by, for example, Demoulin (*Mol. Cell. Biol.* 16:4710-4716, 1996). Still another preferred expression vector is an adenovirus, described by Stratford-Perricaudet, which is defective for E1 and E3 proteins (*J. Clin. Invest.* 90:626-630, 1992). The use of the adenovirus as an Adeno.P1A recombinant for the expression of an antigen is disclosed by Warnier et al., in intradermal injection in mice for immunization against P1A (*Int. J. Cancer*, 67:303-310, 1996). Additional vectors for delivery of nucleic acid are provided below.

The invention also embraces so-called expression kits, which allow the artisan to prepare a desired expression vector or vectors. Such expression kits include at least separate portions of a vector and one or more of the previously discussed breast cancer associated antigen nucleic acid molecules. Other components may be added, as desired, as long as the previously mentioned nucleic acid molecules, which are required, are included. The invention also includes kits for amplification of a breast cancer associated antigen nucleic acid, including at least one pair of amplification primers which hybridize to a breast cancer associated antigen nucleic acid. The primers preferably are 12-32 nucleotides in length and are non-overlapping to prevent formation of "primer-dimers". One of the primers will hybridize to one strand of the breast cancer associated antigen nucleic acid and the second primer will hybridize to the complementary strand of the breast cancer associated antigen nucleic acid, in an arrangement which permits amplification of the breast cancer associated antigen nucleic acid. Selection of appropriate primer pairs is standard in the art. For example, the selection can be made with assistance of a computer program designed for such a purpose, optionally followed by testing the primers for amplification specificity and efficiency.

The invention also permits the construction of cancer associated antigen gene "knock-outs" in cells and in animals, providing materials for studying certain aspects of cancer and immune system responses to cancer.

The invention also provides isolated polypeptides (including whole proteins and partial

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proteins) encoded by the foregoing cancer associated antigen nucleic acids. Such polypeptides are useful, for example, alone or as fusion proteins to generate antibodies, as components of an immunoassay or diagnostic assay or as therapeutics. Cancer associated antigen polypeptides can be isolated from biological samples including tissue or cell homogenates, and can also be expressed recombinantly in a variety of prokaryotic and eukaryotic expression systems by constructing an expression vector appropriate to the expression system, introducing the expression vector into the expression system, and isolating the recombinantly expressed protein. Short polypeptides, including antigenic peptides (such as are presented by MHC molecules on the surface of a cell for immune recognition) also can be synthesized chemically using well-established methods of peptide synthesis.

A unique fragment of a cancer associated antigen polypeptide, in general, has the features and characteristics of unique fragments as discussed above in connection with nucleic acids. As will be recognized by those skilled in the art, the size of the unique fragment will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain. Thus, some regions of breast cancer associated antigens will require longer segments to be unique while others will require only short segments, typically between 5 and 12 amino acids (e.g. 5, 6, 7, 8, 9, 10, 11 or 12 or more, including each integer up to the full length, amino acids long).

Unique fragments of a polypeptide preferably are those fragments which retain a distinct functional capability of the polypeptide. Functional capabilities which can be retained in a unique fragment of a polypeptide include interaction with antibodies, interaction with other polypeptides or fragments thereof, selective binding of nucleic acids or proteins, and enzymatic activity. One important activity is the ability to act as a signature for identifying the polypeptide. Another is the ability to complex with HLA and to provoke in a human an immune response. Those skilled in the art are well versed in methods for selecting unique amino acid sequences, typically on the basis of the ability of the unique fragment to selectively distinguish the sequence of interest from non-family members. A comparison of the sequence of the fragment to those on known databases typically is all that is necessary.

The invention embraces variants of the cancer associated antigen polypeptides described above. As used herein, a "variant" of a cancer associated antigen polypeptide is a polypeptide which contains one or more modifications to the primary amino acid sequence of a cancer associated antigen polypeptide. Modifications which create a cancer associated antigen variant can be made to

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a cancer associated antigen polypeptide 1) to reduce or eliminate an activity of a cancer associated antigen polypeptide; 2) to enhance a property of a cancer associated antigen polypeptide, such as protein stability in an expression system or the stability of protein-protein binding; 3) to provide a novel activity or property to a cancer associated antigen polypeptide, such as addition of an antigenic epitope or addition of a detectable moiety; or 4) to provide equivalent or better binding to an HLA molecule. Modifications to a cancer associated antigen polypeptide are typically made to the nucleic acid which encodes the cancer associated antigen polypeptide, and can include deletions, point mutations, truncations, amino acid substitutions and additions of amino acids or non-amino acid moieties. Alternatively, modifications can be made directly to the polypeptide, such as by cleavage, addition of a linker molecule, addition of a detectable moiety, such as biotin, addition of a fatty acid, and the like. Modifications also embrace fusion proteins comprising all or part of the cancer associated antigen amino acid sequence. One of skill in the art will be familiar with methods for predicting the effect on protein conformation of a change in protein sequence, and can thus "design" a variant cancer associated antigen polypeptide according to known methods. One example of such a method is described by Dahiyat and Mayo in Science 278:82-87, 1997, whereby proteins can be designed de novo. The method can be applied to a known protein to vary a only a portion of the polypeptide sequence. By applying the computational methods of Dahiyat and Mayo, specific variants of a cancer associated antigen polypeptide can be proposed and tested to determine whether the variant retains a desired conformation.

In general, variants include cancer associated antigen polypeptides which are modified specifically to alter a feature of the polypeptide unrelated to its desired physiological activity. For example, cysteine residues can be substituted or deleted to prevent unwanted disulfide linkages. Similarly, certain amino acids can be changed to enhance expression of a breast cancer associated antigen polypeptide by eliminating proteolysis by proteases in an expression system (e.g., dibasic amino acid residues in yeast expression systems in which KEX2 protease activity is present).

Mutations of a nucleic acid which encode a cancer associated antigen polypeptide preferably preserve the amino acid reading frame of the coding sequence, and preferably do not create regions in the nucleic acid which are likely to hybridize to form secondary structures, such a hairpins or loops, which can be deleterious to expression of the variant polypeptide.

Mutations can be made by selecting an amino acid substitution, or by random mutagenesis of

a selected site in a nucleic acid which encodes the polypeptide. Variant polypeptides are then expressed and tested for one or more activities to determine which mutation provides a variant polypeptide with the desired properties. Further mutations can be made to variants (or to non-variant cancer associated antigen polypeptides) which are silent as to the amino acid sequence of the polypeptide, but which provide preferred codons for translation in a particular host. The preferred codons for translation of a nucleic acid in, e.g., *E. coli*, are well known to those of ordinary skill in the art. Still other mutations can be made to the noncoding sequences of a cancer associated antigen gene or cDNA clone to enhance expression of the polypeptide. The activity of variants of cancer associated antigen polypeptides can be tested by cloning the gene encoding the variant cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the variant cancer associated antigen polypeptides, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. For example, the variant cancer associated antigen polypeptide can be tested for reaction with autologous or allogeneic sera as disclosed in the Examples. Preparation of other variant polypeptides may favor testing of other activities, as will be known to one of ordinary skill in the art.

The skilled artisan will also realize that conservative amino acid substitutions may be made in cancer associated antigen polypeptides to provide functionally equivalent variants of the foregoing polypeptides, i.e, the variants retain the functional capabilities of the cancer associated antigen polypeptides. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Variants can be prepared according to methods for altering polypeptide sequence known to one of ordinary skill in the art such as are found in references which compile such methods, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York. Exemplary functionally equivalent variants of the cancer associated antigen polypeptides include conservative amino acid substitutions of in the amino acid sequences of SEQ ID proteins disclosed herein. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D.

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For example, upon determining that a peptide derived from a cancer associated antigen polypeptide is presented by an MHC molecule and recognized by CTLs (e.g., as described in the Examples), one can make conservative amino acid substitutions to the amino acid sequence of the peptide, particularly at residues which are thought not to be direct contact points with the MHC molecule. For example, methods for identifying functional variants of HLA class II binding peptides are provided in a published PCT application of Strominger and Wucherpfennig (PCT/US96/03182). Peptides bearing one or more amino acid substitutions also can be tested for concordance with known HLA/MHC motifs prior to synthesis using, e.g. the computer program described by D'Amaro and Drijfhout (D'Amaro et al., *Human Immunol.* 43:13-18, 1995; Drijfhout et al., *Human Immunol.* 43:1-12, 1995). The substituted peptides can then be tested for binding to the MHC molecule and recognition by CTLs when bound to MHC. These variants can be tested for improved stability and are useful, *inter alia*, in vaccine compositions.

Conservative amino-acid substitutions in the amino acid sequence of cancer associated antigen polypeptides to produce functionally equivalent variants of cancer associated antigen polypeptides typically are made by alteration of a nucleic acid encoding a cancer associated antigen polypeptide. Such substitutions can be made by a variety of methods known to one of ordinary skill in the art. For example, amino acid substitutions may be made by PCR-directed mutation, sitedirected mutagenesis according to the method of Kunkel (Kunkel, Proc. Nat. Acad. Sci. U.S.A. 82: 488-492, 1985), or by chemical synthesis of a gene encoding a cancer associated antigen polypeptide. Where amino acid substitutions are made to a small unique fragment of a cancer associated antigen polypeptide, such as an antigenic epitope recognized by autologous or allogeneic sera or cytolytic T lymphocytes, the substitutions can be made by directly synthesizing the peptide. The activity of functionally equivalent fragments of cancer associated antigen polypeptides can be tested by cloning the gene encoding the altered cancer associated antigen polypeptide into a bacterial or mammalian expression vector, introducing the vector into an appropriate host cell, expressing the altered cancer associated antigen polypeptide, and testing for a functional capability of the cancer associated antigen polypeptides as disclosed herein. Peptides which are chemically synthesized can be tested directly for function, e.g., for binding to antisera recognizing associated antigens.

The invention as described herein has a number of uses, some of which are described elsewhere herein. First, the invention permits isolation of the cancer associated antigen protein

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molecules. A variety of methodologies well-known to the skilled practitioner can be utilized to obtain isolated cancer associated antigen molecules. The polypeptide may be purified from cells which naturally produce the polypeptide by chromatographic means or immunological recognition. Alternatively, an expression vector may be introduced into cells to cause production of the polypeptide. In another method, mRNA transcripts may be microinjected or otherwise introduced into cells to cause production of the encoded polypeptide. Translation of mRNA in cell-free extracts such as the reticulocyte lysate system also may be used to produce polypeptide. Those skilled in the art also can readily follow known methods for isolating cancer associated antigen polypeptides. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography and immune-affinity chromatography.

The isolation and identification of cancer associated antigen genes also makes it possible for the artisan to diagnose a disorder characterized by expression of cancer associated antigens. These methods involve determining expression of one or more cancer associated antigen nucleic acids, and/or encoded cancer associated antigen polypeptides and/or peptides derived therefrom. In the former situation, such determinations can be carried out via any standard nucleic acid determination assay, including the polymerase chain reaction, or assaying with labeled hybridization probes. In the latter situation, such determinations can be carried out by screening patient antisera for recognition of the polypeptide.

The invention also makes it possible isolate proteins which bind to cancer associated antigens as disclosed herein, including antibodies and cellular binding partners of the cancer associated antigens. Additional uses are described further herein.

The invention also provides, in certain embodiments, "dominant negative" polypeptides derived from cancer associated antigen polypeptides. A dominant negative polypeptide is an inactive variant of a protein, which, by interacting with the cellular machinery, displaces an active protein from its interaction with the cellular machinery or competes with the active protein, thereby reducing the effect of the active protein. For example, a dominant negative receptor which binds a ligand but does not transmit a signal in response to binding of the ligand can reduce the biological effect of expression of the ligand. Likewise, a dominant negative catalytically-inactive kinase which interacts normally with target proteins but does not phosphorylate the target proteins can reduce phosphorylation of the target proteins in response to a cellular signal. Similarly, a dominant

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negative transcription factor which binds to a promoter site in the control region of a gene but does not increase gene transcription can reduce the effect of a normal transcription factor by occupying promoter binding sites without increasing transcription.

The end result of the expression of a dominant negative polypeptide in a cell is a reduction in function of active proteins. One of ordinary skill in the art can assess the potential for a dominant negative variant of a protein, and using standard mutagenesis techniques to create one or more dominant negative variant polypeptides. For example, given the teachings contained herein of cancer associated antigens, especially those which are similar to known proteins which have known activities, one of ordinary skill in the art can modify the sequence of the cancer associated antigens by site-specific mutagenesis, scanning mutagenesis, partial gene deletion or truncation, and the like. See, e.g., U.S. Patent No. 5,580,723 and Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor Laboratory Press, 1989. The skilled artisan then can test the population of mutagenized polypeptides for diminution in a selected and/or for retention of such an activity. Other similar methods for creating and testing dominant negative variants of a protein will be apparent to one of ordinary skill in the art.

The invention also involves agents such as polypeptides which bind to cancer associated antigen polypeptides. Such binding agents can be used, for example, in screening assays to detect the presence or absence of cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners and in purification protocols to isolated cancer associated antigen polypeptides and complexes of cancer associated antigen polypeptides and their binding partners. Such agents also can be used to inhibit the native activity of the cancer associated antigen polypeptides, for example, by binding to such polypeptides.

The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to cancer associated antigen polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The

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pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an F(ab')₂ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. Thus, for example, PCT International Publication Number WO 92/04381 teaches the production and use of humanized murine RSV antibodies in which at least a portion of the murine FR regions have been replaced by FR regions of human origin. Such antibodies, including fragments of intact antibodies with antigen-binding ability, are often referred to as "chimeric" antibodies.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for F(ab')₂, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous

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human or non-human sequences; chimeric F(ab')₂ fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to cancer associated antigen polypeptides, and complexes of both cancer associated antigen polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the cancer associated antigen polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the cancer associated antigen polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the cancer associated antigen polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the cancer associated antigen polypeptides. Thus, the cancer associated antigen polypeptides of the invention, or a fragment thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the cancer

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associated antigen polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of cancer associated antigen and for other purposes that will be apparent to those of ordinary skill in the art.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express cancer associated antigens or to therapeutically useful agents according to standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium. Other diagnostic agents useful in the invention will be apparent to one of ordinary skill in the art. As used herein, "therapeutically useful agents" include any therapeutic molecule which desirably is targeted selectively to a cell expressing one of the cancer antigens disclosed herein, including antineoplastic agents, radioiodinated compounds, toxins, other cytostatic or cytolytic drugs, and so forth. Antineoplastic therapeutics are well known and include: aminoglutethimide, azathioprine, bleomycin sulfate, busulfan, carmustine, chlorambucil, cisplatin, cyclophosphamide, cyclosporine, cytarabidine, dacarbazine, dactinomycin, daunorubicin, doxorubicin, taxol, etoposide, fluorouracil, interferon-α, lomustine, mercaptopurine, methotrexate, mitotane, procarbazine HCl, thioguanine, vinblastine sulfate and vincristine sulfate. Additional antineoplastic agents include those disclosed in Chapter 52, Antineoplastic Agents (Paul Calabresi and Bruce A. Chabner), and the introduction thereto, 1202-1263, of Goodman and Gilman's "The Pharmacological Basis of Therapeutics", Eighth Edition, 1990, McGraw-Hill, Inc. (Health Professions Division). Toxins can be proteins such as, for example, pokeweed anti-viral protein, cholera toxin, pertussis toxin, ricin, gelonin, abrin, diphtheria exotoxin, or Pseudomonas exotoxin. Toxin moieties can also be high energy-emitting radionuclides such as cobalt-60.

In the foregoing methods, antibodies prepared according to the invention also preferably are specific for the cancer associated antigen/MHC complexes described herein.

When "disorder" is used herein, it refers to any pathological condition where the cancer associated antigens are expressed. An example of such a disorder is cancer, breast, colon, gastric,

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renal, prostate and lung cancers as particular examples.

Samples of tissue and/or cells for use in the various methods described herein can be obtained through standard methods such as tissue biopsy, including punch biopsy and cell scraping, and collection of blood or other bodily fluids by aspiration or other methods.

In certain embodiments of the invention, an immunoreactive cell sample is removed from a subject. By "immunoreactive cell" is meant a cell which can mature into an immune cell (such as a B cell, a helper T cell, or a cytolytic T cell) upon appropriate stimulation. Thus immunoreactive cells include CD34⁺ hematopoietic stem cells, immature T cells and immature B cells. When it is desired to produce cytolytic T cells which recognize a cancer associated antigen, the immunoreactive cell is contacted with a cell which expresses a cancer associated antigen under conditions favoring production, differentiation and/or selection of cytolytic T cells; the differentiation of the T cell precursor into a cytolytic T cell upon exposure to antigen is similar to clonal selection of the immune system.

Some therapeutic approaches based upon the disclosure are premised on a response by a subject's immune system, leading to lysis of antigen presenting cells, such as breast cancer cells which present one or more cancer associated antigens. One such approach is the administration of autologous CTLs specific to a cancer associated antigen/MHC complex to a subject with abnormal cells of the phenotype at issue. It is within the ability of one of ordinary skill in the art to develop such CTLs *in vitro*. An example of a method for T cell differentiation is presented in International Application number PCT/US96/05607. Generally, a sample of cells taken from a subject, such as blood cells, are contacted with a cell presenting the complex and capable of provoking CTLs to proliferate. The target cell can be a transfectant, such as a COS cell of the type described herein. These transfectants present the desired complex of their surface and, when combined with a CTL of interest, stimulate its proliferation. COS cells, such as those used herein are widely available, as are other suitable host cells. Specific production of a CTL clone is described herein, and is well known in the art. The clonally expanded autologous CTLs then are administered to the subject.

Another method for selecting antigen-specific CTL clones has recently been described (Altman et al., Science 274:94-96, 1996; Dunbar et al., Curr. Biol. 8:413-416, 1998), in which fluorogenic tetramers of MHC class I molecule/peptide complexes are used to detect specific CTL clones. Briefly, soluble MHC class I molecules are folded *in vitro* in the presence of β₂-

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microglobulin and a peptide antigen which binds the class I molecule. After purification, the MHC/peptide complex is purified and labeled with biotin. Tetramers are formed by mixing the biotinylated peptide-MHC complex with labeled avidin (e.g. phycoerythrin) at a molar ratio or 4:1. Tetramers are then contacted with a source of CTLs such as peripheral blood or lymph node. The tetramers bind CTLs which recognize the peptide antigen/MHC class I complex. Cells bound by the tetramers can be sorted by fluorescence activated cell sorting to isolate the reactive CTLs. The isolated CTLs then can be expanded *in vitro* for use as described herein.

To detail a therapeutic methodology, referred to as adoptive transfer (Greenberg, *J. Immunol*. 136(5): 1917, 1986; Riddel et al., *Science* 257: 238, 1992; Lynch et al, *Eur. J. Immunol*. 21: 1403-1410,1991; Kast et al., *Cell* 59: 603-614, 1989), cells presenting the desired complex are combined with CTLs leading to proliferation of the CTLs specific thereto. The proliferated CTLs are then administered to a subject with a cellular abnormality which is characterized by certain of the abnormal cells presenting the particular complex. The CTLs then lyse the abnormal cells, thereby achieving the desired therapeutic goal.

The foregoing therapy assumes that at least some of the subject's abnormal cells present the relevant HLA cancer associated antigen complex. This can be determined very easily, as the art is very familiar with methods for identifying cells which present a particular HLA molecule, as well as how to identify cells expressing DNA of the pertinent sequences, in this case a cancer associated antigen sequence. Once cells presenting the relevant complex are identified via the foregoing screening methodology, they can be combined with a sample from a patient, where the sample contains CTLs. If the complex presenting cells are lysed by the mixed CTL sample, then it can be assumed that a cancer associated antigen is being presented, and the subject is an appropriate candidate for the therapeutic approaches set forth *supra*.

Adoptive transfer is not the only form of therapy that is available in accordance with the invention. CTLs can also be provoked *in vivo*, using a number of approaches. One approach is the use of non-proliferative cells expressing the complex. The cells used in this approach may be those that normally express the complex, such as irradiated tumor cells or cells transfected with one or both of the genes necessary for presentation of the complex (i.e. the antigenic peptide and the presenting HLA molecule). Chen et al. (*Proc. Natl. Acad. Sci. USA* 88: 110-114,1991) exemplifies this approach, showing the use of transfected cells expressing HPVE7 peptides in a therapeutic

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regime. Various cell types may be used. Similarly, vectors carrying one or both of the genes of interest may be used. Viral or bacterial vectors are especially preferred. For example, nucleic acids which encode a breast cancer associated antigen polypeptide or peptide may be operably linked to promoter and enhancer sequences which direct expression of the cancer associated antigen polypeptide or peptide in certain tissues or cell types. The nucleic acid may be incorporated into an expression vector. Expression vectors may be unmodified extrachromosomal nucleic acids, plasmids or viral genomes constructed or modified to enable insertion of exogenous nucleic acids, such as those encoding cancer associated antigen, as described elsewhere herein. Nucleic acids encoding a cancer associated antigen also may be inserted into a retroviral genome, thereby facilitating integration of the nucleic acid into the genome of the target tissue or cell type. In these systems, the gene of interest is carried by a microorganism, e.g., a Vaccinia virus, retrovirus or adenovirus, and the materials de facto "infect" host cells. The cells which result present the complex of interest, and are recognized by autologous CTLs, which then proliferate.

A similar effect can be achieved by combining the cancer associated antigen or a stimulatory fragment thereof with an adjuvant to facilitate incorporation into antigen presenting cells *in vivo*. The breast cancer associated antigen polypeptide is processed to yield the peptide partner of the HLA molecule while a cancer associated antigen peptide may be presented without the need for further processing. Generally, subjects can receive an intradermal injection of an effective amount of the cancer associated antigen. Initial doses can be followed by booster doses, following immunization protocols standard in the art. Preferred cancer associated antigens include those found to react with allogeneic cancer antisera, such as the nucleic acids (and encoded polypeptides and peptides) of SEQ ID NO:31,33 and 34 and others, for example, shown in the examples below.

The invention involves the use of various materials disclosed herein to "immunize" subjects or as "vaccines". As used herein, "immunization" or "vaccination" means increasing or activating an immune response against an antigen. It does not require elimination or eradication of a condition but rather contemplates the clinically favorable enhancement of an immune response toward an antigen. Generally accepted animal models can be used for testing of immunization against breast cancer using a cancer associated antigen nucleic acid. For example, cancer cells can be introduced into a mouse to create a tumor, and one or more cancer associated antigen nucleic acids can be delivered by the methods described herein. The effect on the cancer cells (e.g., reduction of tumor

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size) can be assessed as a measure of the effectiveness of the cancer associated antigen nucleic acid immunization. Of course, testing of the foregoing animal model using more conventional methods for immunization include the administration of one or more cancer associated antigen polypeptides or peptides derived therefrom, optionally combined with one or more adjuvants and/or cytokines to boost the immune response. Methods for immunization, including formulation of a vaccine composition and selection of doses, route of administration and the schedule of administration (e.g. primary and one or more booster doses), are well known in the art. The tests also can be performed in humans, where the end point is to test for the presence of enhanced levels of circulating CTLs against cells bearing the antigen, to test for levels of circulating antibodies against the antigen, to test for the presence of cells expressing the antigen and so forth.

As part of the immunization compositions, one or more cancer associated antigens or stimulatory fragments thereof are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL. SmithKline Beecham), a congener obtained after purification and acid hydrolysis of Salmonella minnesota Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from Quillja saponaria extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); OS-7, OS-17, OS-18, and OS-L1 (So et al., Mol. Cells 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Preferably, the peptides are administered mixed with a combination of DQS21/MPL. The ratio of DQS21 to MPL typically will be about 1:10 to 10:1, preferably about 1:5 to 5:1 and more preferably about 1:1. Typically for human administration, DQS21 and MPL will be present in a vaccine formulation in the range of about 1 µg to about 100 µg. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, Monoclonal Antibodies: Principles and Practice, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

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Other agents which stimulate the immune response of the subject can also be administered to the subject. For example, other cytokines are also useful in vaccination protocols as a result of their lymphocyte regulatory properties. Many other cytokines useful for such purposes will be known to one of ordinary skill in the art, including interleukin-12 (IL-12) which has been shown to enhance the protective effects of vaccines (*see*, *e.g.*, *Science* 268: 1432-1434, 1995), GM-CSF and IL-18. Thus cytokines can be administered in conjunction with antigens and adjuvants to increase the immune response to the antigens.

There are a number of immune response potentiating compounds that can be used in vaccination protocols. These include costimulatory molecules provided in either protein or nucleic acid form. Such costimulatory molecules include the B7-1 and B7-2 (CD80 and CD86 respectively) molecules which are expressed on dendritic cells (DC) and interact with the CD28 molecule expressed on the T cell. This interaction provides costimulation (signal 2) to an antigen/MHC/TCR stimulated (signal 1) T cell, increasing T cell proliferation and effector function. B7 also interacts with CTLA4 (CD152) on T cells and studies involving CTLA4 and B7 ligands indicate that the B7-CTLA4 interaction can enhance antitumor immunity and CTL proliferation, Zheng P., et al. *PNAS* 95 (11) 6284-6289 (1998).

B7 typically is not expressed on tumor cells so they are not efficient antigen presenting cells (APCs) for T cells. Induction of B7 expression would enable the tumor cells to stimulate more efficiently CTL proliferation and effector function. A combination of B7/IL-6/IL-12 costimulation has been shown to induce IFN-gamma and a Th1 cytokine profile in the T cell population leading to further enhanced T cell activity, Gajewski et al., *J. I mmunol*, 154:5637-5648 (1995). Tumor cell transfection with B7 has ben discussed in relation to *in vitro* CTL expansion for adoptive transfer immunotherapy by Wang et al., J Immunol, 19:1-8 (1986). Other delivery mechanisms for the B7 molecule would include nucleic acid (naked DNA) immunization Kim J., et al. *Nat Biotechnol.*, 15:7:641-646 (1997) and recombinant viruses such as adeno and pox (Wendtner et al., *Gene Ther*, 4:7:726-735 (1997)). These systems are all amenable to the construction and use of expression cassettes for the coexpression of B7 with other molecules of choice such as the antigens or fragment(s) of antigens discussed herein (including polytopes) or cytokines. These delivery systems can be used for induction of the appropriate molecules *in vitro* and for *in vivo* vaccination situations.

The use of anti-CD28 antibodies to directly stimulate T cells in vitro and in vivo could also be

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considered.

Lymphocyte function associated antigen-3 (LFA-3) is expressed on APCs and some tumor cells and interacts with CD2 expressed on T cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Parra et al., *J. Immunol.*, 158:637-642 (1997), Fenton et al., *J. Immunother*, 21:2:95-108 (1989).

Lymphocyte function associated antigen-1 (LFA-1) is expressed on leukocytes and interacts with ICAM-1 expressed on APCs and some tumor cells. This interaction induces T cell IL-2 and IFN-gamma production and can thus complement but not substitute, the B7/CD28 costimulatory interaction, Fenton et al., *J. Immunothera*, 21:2:95-108 (1998). LFA-1 is thus a further example of a costimulatory molecule that could be provided in a vaccination protocol in the various ways discussed above for B7.

Complete CTL activation and effector function requires Th cell help through the interaction between the Th cell CD40L (CD40 ligand) molecule and the CD40 molecule expressed by DCS, Ridge et al., *Nature*, 393:474 (1998), Bennett et al., *Nature*, 393:478 (1998), Schoenberger et al., *Nature*, 393:480 (1998). This mechanism of this costimulatory signal is likely to involve upregulation of B7 and associated IL-6/IL-12 production by the DC (APC). The CD40-CD40L interaction thus complements the signal 1 (antigen/MHC-TCR) and signal 2 (B7-CD28) interactions.

The use of anti-CD40 antibodies to stimulate DC cells directly, would be expected to enhance a response to tumor antigens which are normally encountered outside of a inflammatory context or are presented by non-professional APCs (tumor cells). In these situations Th help and B7 costimulation signals are not provided. This mechanism might be used in the context of antigen pulsed DC based therapies or in situations where Th epitopes have not been defined within known TRA precursors.

A cancer associated antigen polypeptide, or a fragment thereof, also can be used to isolate their native binding partners. Isolation of such binding partners may be performed according to well-known methods. For example, isolated cancer associated antigen polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, or a filter), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner which can interact with cancer associated antigen polypeptides is present in the solution,

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then it will bind to the substrate-bound cancer associated antigen polypeptide. The binding partner then may be isolated.

It will also be recognized that the invention embraces the use of the cancer associated antigen cDNA sequences in expression vectors, as well as to transfect host cells and cell lines, be these prokaryotic (e.g., *E. coli*), or eukaryotic (e.g., dendritic cells, B cells, CHO cells, COS cells, yeast expression systems and recombinant baculovirus expression in insect cells). Especially useful are mammalian cells such as human, mouse, hamster, pig, goat, primate, etc. They may be of a wide variety of tissue types, and include primary cells and cell lines. Specific examples include keratinocytes, peripheral blood leukocytes, bone marrow stem cells and embryonic stem cells. The expression vectors require that the pertinent sequence, i.e., those nucleic acids described *supra*, be operably linked to a promoter.

The invention also contemplates delivery of nucleic acids, polypeptides or peptides for vaccination. Delivery of polypeptides and peptides can be accomplished according to standard vaccination protocols which are well known in the art. In another embodiment, the delivery of nucleic acid is accomplished by *ex vivo* methods, i.e. by removing a cell from a subject, genetically engineering the cell to include a breast cancer associated antigen, and reintroducing the engineered cell into the subject. One example of such a procedure is outlined in U.S. Patent 5,399,346 and in exhibits submitted in the file history of that patent, all of which are publicly available documents. In general, it involves introduction *in vitro* of a functional copy of a gene into a cell(s) of a subject, and returning the genetically engineered cell(s) to the subject. The functional copy of the gene is under operable control of regulatory elements which permit expression of the gene in the genetically engineered cell(s). Numerous transfection and transduction techniques as well as appropriate expression vectors are well known to those of ordinary skill in the art, some of which are described in PCT application WO95/00654. *In vivo* nucleic acid delivery using vectors such as viruses and targeted liposomes also is contemplated according to the invention.

In preferred embodiments, a virus vector for delivering a nucleic acid encoding a cancer associated antigen is selected from the group consisting of adenoviruses, adeno-associated viruses, poxviruses including vaccinia viruses and attenuated poxviruses, Semliki Forest virus, Venezuelan equine encephalitis virus, retroviruses, Sindbis virus, and Ty virus-like particle. Examples of viruses and virus-like particles which have been used to deliver exogenous nucleic acids include:

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replication-defective adenoviruses (e.g., Xiang et al., *Virology* 219:220-227, 1996; Eloit et al., *J. Virol* 7:5375-5381, 1997; Chengalvala et al., *Vaccine* 15:335-339, 1997), a modified retrovirus (Townsend et al., *J. Virol*. 71:3365-3374, 1997), a nonreplicating retrovirus (Irwin et al., *J. Virol*. 68:5036-5044, 1994), a replication defective Semliki Forest virus (Zhao et al., *Proc. Natl. Acad. Sci. USA* 92:3009-3013, 1995), canarypox virus and highly attenuated vaccinia virus derivative (Paoletti, *Proc. Natl. Acad. Sci. USA* 93:11349-11353, 1996), non-replicative vaccinia virus (Moss, *Proc. Natl. Acad. Sci. USA* 93:11341-11348, 1996), replicative vaccinia virus (Moss, *Dev. Biol. Stand.* 82:55-63, 1994), Venzuelan equine encephalitis virus (Davis et al., *J. Virol.* 70:3781-3787, 1996), Sindbis virus (Pugachev et al., *Virology* 212:587-594, 1995), and Ty virus-like particle (Allsopp et al., *Eur J. Immunol* 26:1951-1959, 1996). In preferred embodiments, the virus vector is an adenovirus.

Another preferred virus for certain applications is the adeno-associated virus, a double-stranded DNA virus. The adeno-associated virus is capable of infecting a wide range of cell types and species and can be engineered to be replication-deficient. It further has advantages, such as heat and lipid solvent stability, high transduction frequencies in cells of diverse lineages, including hematopoietic cells, and lack of superinfection inhibition thus allowing multiple series of transductions. The adeno-associated virus can integrate into human cellular DNA in a site-specific manner, thereby minimizing the possibility of insertional mutagenesis and variability of inserted gene expression. In addition, wild-type adeno-associated virus infections have been followed in tissue culture for greater than 100 passages in the absence of selective pressure, implying that the adeno-associated virus genomic integration is a relatively stable event. The adeno-associated virus can also function in an extrachromosomal fashion.

In general, other preferred viral vectors are based on non-cytopathic eukaryotic viruses in which non-essential genes have been replaced with the gene of interest. Non-cytopathic viruses include retroviruses, the life cycle of which involves reverse transcription of genomic viral RNA into DNA with subsequent proviral integration into host cellular DNA. Adenoviruses and retroviruses have been approved for human gene therapy trials. In general, the retroviruses are replication-deficient (i.e., capable of directing synthesis of the desired proteins, but incapable of manufacturing an infectious particle). Such genetically altered retroviral expression vectors have general utility for the high-efficiency transduction of genes *in vivo*. Standard protocols for

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producing replication-deficient retroviruses (including the steps of incorporation of exogenous genetic material into a plasmid, transfection of a packaging cell lined with plasmid, production of recombinant retroviruses by the packaging cell line, collection of viral particles from tissue culture media, and infection of the target cells with viral particles) are provided in Kriegler, M., "Gene Transfer and Expression, A Laboratory Manual," W.H. Freeman C.O., New York (1990) and Murry, E.J. Ed. "Methods in Molecular Biology," vol. 7, Humana Press, Inc., Cliffton, New Jersey (1991).

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Preferably the foregoing nucleic acid delivery vectors: (1) contain exogenous genetic material that can be transcribed and translated in a mammalian cell and that can induce an immune response in a host, and (2) contain on a surface a ligand that selectively binds to a receptor on the surface of a target cell, such as a mammalian cell, and thereby gains entry to the target cell.

Various techniques may be employed for introducing nucleic acids of the invention into cells, depending on whether the nucleic acids are introduced in vitro or in vivo in a host. Such techniques include transfection of nucleic acid-CaPO4 precipitates, transfection of nucleic acids associated with DEAE, transfection or infection with the foregoing viruses including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. Preferred antibodies include antibodies which selectively bind a cancer associated antigen, alone or as a complex with a MHC molecule. Especially preferred are monoclonal antibodies. Where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

When administered, the therapeutic compositions of the present invention can be

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administered in pharmaceutically acceptable preparations. Such preparations may routinely contain pharmaceutically acceptable concentrations of salt, buffering agents, preservatives, compatible carriers, supplementary immune potentiating agents such as adjuvants and cytokines and optionally other therapeutic agents.

The therapeutics of the invention can be administered by any conventional route, including injection or by gradual infusion over time. The administration may, for example, be oral, intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous, or transdermal. When antibodies are used therapeutically, a preferred route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing antibodies are well known to those of skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694-1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing antibody aerosols without resort to undue experimentation. When using antisense preparations of the invention, slow intravenous administration is preferred.

The compositions of the invention are administered in effective amounts. An "effective amount" is that amount of a cancer associated antigen composition that alone, or together with further doses, produces the desired response, e.g. increases an immune response to the cancer associated antigen. In the case of treating a particular disease or condition characterized by expression of one or more cancer associated antigens, such as cancer, the desired response is inhibiting the progression of the disease. This may involve only slowing the progression of the disease temporarily, although more preferably, it involves halting the progression of the disease permanently. This can be monitored by routine methods or can be monitored according to diagnostic methods of the invention discussed herein. The desired response to treatment of the disease or condition also can be delaying the onset or even preventing the onset of the disease or condition.

Such amounts will depend, of course, on the particular condition being treated, the severity of the condition, the individual patient parameters including age, physical condition, size and weight, the duration of the treatment, the nature of concurrent therapy (if any), the specific route of

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administration and like factors within the knowledge and expertise of the health practioner. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is generally preferred that a maximum dose of the individual components or combinations thereof be used, that is, the highest safe dose according to sound medical judgment. It will be understood by those of ordinary skill in the art, however, that a patient may insist upon a lower dose or tolerable dose for medical reasons, psychological reasons or for virtually any other reasons.

The pharmaceutical compositions used in the foregoing methods preferably are sterile and contain an effective amount of breast cancer associated antigen or nucleic acid encoding cancer associated antigen for producing the desired response in a unit of weight or volume suitable for administration to a patient. The response can, for example, be measured by determining the immune response following administration of the cancer associated antigen composition via a reporter system as described herein, by measuring downstream effects such as gene expression, or by measuring the physiological effects of the breast cancer associated antigen composition, such as regression of a tumor or decrease of disease symptoms. Other assays will be known to one of ordinary skill in the art and can be employed for measuring the level of the response.

The doses of cancer associated antigen compositions (e.g., polypeptide, peptide, antibody, cell or nucleic acid) administered to a subject can be chosen in accordance with different parameters, in particular in accordance with the mode of administration used and the state of the subject. Other factors include the desired period of treatment. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

In general, for treatments for eliciting or increasing an immune response, doses of cancer associated antigen are formulated and administered in doses between 1 ng and 1 mg, and preferably between 10 ng and 100 μ g, according to any standard procedure in the art. Where nucleic acids encoding cancer associated antigen of variants thereof are employed, doses of between 1 ng and 0.1 mg generally will be formulated and administered according to standard procedures. Other protocols for the administration of cancer associated antigen compositions will be known to one of ordinary skill in the art, in which the dose amount, schedule of injections, sites of injections, mode of administration (e.g., intra-tumoral) and the like vary from the foregoing. Administration of cancer

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associated antigen compositions to mammals other than humans, e.g. for testing purposes or veterinary therapeutic purposes, is carried out under substantially the same conditions as described above.

As part of the immunization compositions, the peptide antigens are administered with one or more adjuvants to induce an immune response or to increase an immune response. An adjuvant is a substance incorporated into or administered with antigen which potentiates the immune response. Adjuvants may enhance the immunological response by providing a reservoir of antigen (extracellularly or within macrophages), activating macrophages and stimulating specific sets of lymphocytes. Adjuvants of many kinds are well known in the art. Specific examples of adjuvants include monophosphoryl lipid A (MPL, SmithKline Beecham), a congener obtained after purification and acid hydrolysis of Salmonella minnesota Re 595 lipopolysaccharide; saponins including QS21 (SmithKline Beecham), a pure QA-21 saponin purified from Quillja saponaria extract; DQS21, described in PCT application WO96/33739 (SmithKline Beecham); QS-7, QS-17, QS-18, and QS-L1 (So et al., Mol. Cells 7:178-186, 1997); incomplete Freund's adjuvant; complete Freund's adjuvant; montanide; and various water-in-oil emulsions prepared from biodegradable oils such as squalene and/or tocopherol. Other adjuvants are known in the art and can be used in the invention (see, e.g. Goding, Monoclonal Antibodies: Principles and Practice, 2nd Ed., 1986). Methods for the preparation of mixtures or emulsions of peptide and adjuvant are well known to those of skill in the art of vaccination.

Where cancer associated antigen peptides are used for vaccination, modes of administration which effectively deliver the cancer associated antigen and adjuvant, such that an immune response to the antigen is increased, can be used. For administration of a cancer associated antigen peptide in adjuvant, preferred methods include intradermal, intravenous, intramuscular and subcutaneous administration. Although these are preferred embodiments, the invention is not limited by the particular modes of administration disclosed herein. Standard references in the art (e.g., Remington's Pharmaceutical Sciences, 18th edition, 1990) provide modes of administration and formulations for delivery of immunogens with adjuvant or in a non-adjuvant carrier.

When administered, the pharmaceutical preparations of the invention are applied in pharmaceutically-acceptable amounts and in pharmaceutically-acceptable compositions. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the

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effectiveness of the biological activity of the active ingredients. Such preparations may routinely contain salts, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically-acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically-acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically-acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

A breast cancer associated antigen composition may be combined, if desired, with a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" as used herein means one or more compatible solid or liquid fillers, diluents or encapsulating substances which are suitable for administration into a human. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions also are capable of being co-mingled with the molecules of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

The pharmaceutical compositions may contain suitable buffering agents, including: acetic acid in a salt; citric acid in a salt; boric acid in a salt; and phosphoric acid in a salt.

The pharmaceutical compositions also may contain, optionally, suitable preservatives, such as: benzalkonium chloride; chlorobutanol; parabens and thimerosal.

The pharmaceutical compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well-known in the art of pharmacy. All methods include the step of bringing the active agent into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the active compound into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

Compositions suitable for oral administration may be presented as discrete units, such as

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capsules, tablets, lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion.

Compositions suitable for parenteral administration conveniently comprise a sterile aqueous or non-aqueous preparation of breast cancer associated antigen polypeptides or nucleic acids, which is preferably isotonic with the blood of the recipient. This preparation may be formulated according to known methods using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation also may be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example, as a solution in 1,3-butane diol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono-or di-glycerides. In addition, fatty acids such as oleic acid may be used in the preparation of injectables. Carrier formulation suitable for oral, subcutaneous, intravenous, intramuscular, etc. administrations can be found in *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA.

Examples

Example 1: Preparation of breast cancer cDNA expression libraries

Step 1: Purification of total RNA from tumors.

Total RNA was isolated from tumor samples using the guanidium thiocyanate-phenol-chloroform extraction protocol described by Chomczynski and Sacci (*Anal. Biochem.* 162:156-159, 1987).

Step 2: Purification of mRNA.

A Dynabeads mRNA isolation kit (Dynal, Cat.No. 610.01) was used to isolate mRNA from the pool of total RNA isolated in step 1 above according to the manufacturer's instructions.

Step 3: cDNA synthesis.

cDNA synthesis was performed using a ZAP-cDNA synthesis Kit (Stratagene, La Jolla CA; Cat. No. 200400) according to the manufacturer's protocol. A specific linker-primer which contains a XbaI cloning site was designed and used in this protocol, to facilitate subcloning into TriplEx

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vector. The sequence of the primer was:

Step 4: Ligation into the TriplEx vector arms.

The cDNAs generated in step 3 above were ligated into TriplEx vector arms (Clontech, Palo Alto, CA; Cat. No. 6162-1); the arms were predigested with EcoR I/Xba I.

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Step 5: Packaging into phages with Gigapack III kit.

The ligation mix (TriplEx/cDNA) from step 4 was packed into phages using the Gigapack III Gold Cloning Kit (Stratagene, Cat. N.200450) according to the protocol supplied with the kit.

Step 6: Titering and amplification of generated libraries was performed accoding to the Stratagene protocols.

The foregoing protocol was used to prepare several libraries from tumor sample of different patients. Some libraries were prepared using the UNI-ZAP XR vector system (Stratagene) according to the manufacturer's protocol, and some using the TriplEx system as described above.

Table 2

UNI-ZAP Libraries		
Code for tumors	Titer of the library	Histopathological diagnosis
HBR173	1.8 x 10 ⁶ pfu	Ductal Carcinoma, Grade III
HBR184	3.5 x 10 ⁶ pfu	Invasive Ductal Carcinoma, Grade II
TriplEx libraries		
Code for tumors	Titer of the library	Histopoathological diagnosis
HBR173	2.3 x 10 ⁶ pfu	Ductal Carcinoma, Grade III
HBR184	1.1 x 10 ⁶ pfu	Ivasive Ductal Carcinoma, Grade II
HBR257	2.5 x 10 ⁶ pfu	Invasive Ductal Carcinoma, Grade II
HBR297	4.0 x 10 ⁶ pfu	Ductal Carcinoma, Grade II
HBR248	1.0 x 10 ⁶ pfu	Invasive Ductal Carcinoma with
		Vascular Permeation, Grade III

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HBR271	2.5 x 10 ⁶ pfu	Medullary Carcimoma
HBR263	10.0 x 10 ⁶ pfu	Inv. Pleiomorphic Lobular Carcinoma,
		Grade II

All libraries were screened with the exception of HBR173 (no autologous serum). No serum-positive clones were found by screening HBR271 library.

Example 2: Immunoscreening

Sera was obtained from donors undergoing routine diagnostic and therapeutic procedures. It was stored at - 70°C prior to absorption. Sera, at a dilution of 1:10 in Tris buffered saline (TBS, pH 7.5), was sequentially passed through Sepharose 4B columns which had been coupled to lysates from E. coli Y1090 and bacteriophage infected E. coli BNN97 (5 Prime 3 Prime, Inc. Boulder, Co.). Final serum dilutions were prepared in 0.2% non-fat dried milk/TBS (NFDM) and stored at 4°C. Library screening was performed as described by Sahin et al. (Proc. Natl. Acad. Sci. USA 92:11810-11813, 1995) with following modifications. Recombinant phage at a concentration of 4 x 10³ per 15 cm plate were amplified for 6 hours and transferred to nitrocellulose membranes for an additional 15 hours at 37°C. Membranes were then blocked with 5% NFDM. As an alternative to generation of IgG subtracted libraries, membranes were pre-screened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific, goat anti-human IgG (Jackson Immunoresearch Laboratories Inc., West Grove, PA) for 1 hour at room temperature. Color was developed with 3.3' diaminobenzidine tetrahydrochloride and IgG encoding clones were scored. Membranes were then incubated in a 1:100 dilution of absorbed autologous sera for 15 hours at room temperature. Following serum exposure, filters were incubated in a 1:3000 dilution of alkaline phosphatase conjugated, Fc fragment specific, goat anti-human IgG (Jackson Immunoresearch Laboratories Inc.) for 1 hour at room temperature and processed for 4-nitro blue tetrazolium chloride/5-bromo-4-chloro- 3-indolyl-phosphate color development. Serum positive clones were subcloned and retested for serum reactivity as above except nitrocellulose transfer was decreased to 3 hours. For the determination of allogeneic serum reactivity, plates containing an equal number of serum positive clones and negative control plaques were similarly processed less the IgG prescreening steps. A minimum of 5 x 10⁵ recombinants were screened per cDNA library, a number

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which approximates a point at which the likelihood of repeat isolations of previously identified clones outweigh the prospect of identifying new clones.

Example 3: DNA Sequencing

Phage cDNA clones were converted to pBKCMV phagemid forms by in vivo excision. Plasmid DNA was purified on Qiaprep spin columns (Qiagen Inc. Chatsworth, CA) and subjected to EcoRI/XbaI restriction enzyme digestion. Clones representing different cDNA inserts were sequenced at Cornell University DNA services (Ithaca, NY) using an ABI Prism (Perkin Elmer) automated DNA sequencer. The sequences of the clones were compared with sequences in GenBank and HGI databases to detect homologous nucleic acid and/or protein sequences. The following table lists exemplary related sequences.

Table 3: Sequences Related to Breast Cancer Associated Antigen Clones

Clone	Nucleotide Homology	Clone	Nucleotide Homology	Clone	Nucleotide Homology
LONY-Br-1	L34543	LONY-Br-23	AA262134, U74628	LONY-Br-44	D15057
LONY-Br-2	S75417	LONY-Br-24	AA282633	LONY-Br-45	AB000815
LONY-Br-3	J05211	LONY-Br-25	M62324	LONY-Br-46	L04733
LONY-Br-4	X15187	LONY-Br-26	M99389	LONY-Br-47	X88791
LONY-Br-5	X62083	LONY-Br-27	X79389	LONY-Br-48	AF000430
LONY-Br-6	J04965	LONY-Br-28	.D44466	LONY-Br-49	none
LONY-Br-7	D63784	LONY-Br-29	M33197	LONY-Br-50	AA226732
LONY-Br-8	U11 29 2	LONY-Br-30	M17886	LONY-Br-51	AA046574
LONY-Br-9	HSB06D102	LONY-Br-31	L38941	LONY-Br-52	none
LONY-Br-10	none	LONY-Br-32	X17644	LONY-Br-53	AB002307
LONY-Br-11	none	LONY-Br-33	X75342	92	AA127328
LONY-Br-12	AA430998	LONY-Br-33	X75342	101	AA167314
LONY-Br-13	D83032	LONY-Br-34	U43368	102	AA508139
LONY-Br-14	AA034417	LONY-Br-35	X15882	107	none
LONY-Br-15	AA167070	LONY-Br-37	AA121558	109	AA220229

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LONY-Br-16	none	LONY-Br-38	AA211771	110	W67775
LONY-Br-17	AA161103	LONY-Br-39	AA367417	111	AA280070
LONY-Br-19	R13835	LONY-Br-40	AA188052	112	AF004292
LONY-Br-20	HUMORF003	LONY-Br-41	THC83518	131	none
LONY-Br-21	S74572	LONY-Br-42	none	143	AA481578
LONY-Br-22	AA070233	LONY-Br-43	HU35246	162	AA481578

Example 4: Reverse transcriptase (RT) PCR and Rapid Amplification of cDNA Ends (RACE)

The mRNA expression pattern of selected cDNA clones was determined by RT- PCR using a panel of normal tissue RNA. This test panel consisted of lung, testis, small intestine, colon, breast, liver, and placenta, and was purchased from Clontech Laboratories Inc. (Palo Alto, CA). Colon tumor RNA was also included in this panel and was prepared as described above. As a control for genomic DNA contamination, all cDNA synthesis reactions were set up in duplicate with the additional sample lacking reverse transcriptase. Gene specific PCR primers were designed to amplify 5' fragments of 300-400 bp and were purchased commercially (Gibco BRL, Grand Island, NY). PCR reactions were undertaken at an annealing temperature of 68°C using a Perkin Elmer thermal cycler. In certain cases, RT-PCR products were subcloned into the pCR2.1 plasmid vector (Invitrogen) and multiple clones were subjected to DNA sequencing as described. 5' and 3' RACE reactions were undertaken using gene specific and adapter primers in conjunction with Marathon Ready normal colon cDNA and KlenTaq polymerase (Clontech) as per manufacturers protocol. Products were then subcloned into the pCR2.1 plasmid vector (Invitrogen) and screened by PCR with internal primers for presence of the desired insert. Multiple RACE clones were subjected to DNA sequencing as described.

Example 5: Northern blot analysis

Northern blots containing the transfer yields of 2 μ g poly A⁺ RNA from a panel of normal tissues were obtained commercially (Clontech). Random primed ³²P labeled probes consisting of 300-600 bp PCR products from 5 prime coding sequences of serum positive cDNA clones were hybridized for 1.5 hours in Expresshyb (Clontech) at 68°C and washed at high stringency (2 times,

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30 min. each, 0.1X SSC/0.1% SDS at 68°C). Resultant blots were used to expose Biomax MS autoradiography film (Eastman Kodak Co., Rochester, NY).

Table 4: Breast Cancer Associated Antigen Clone mRNA sizes

Clone	Size (kb)	Clone	Size (kb)	Clone	Size (kb)
LONY-Br-1	1.8	LONY-Br-17	1.0	LONY-Br-33	2.6
LONY-Br-2	2.9	LONY-Br-19	1.5	LONY-Br-34	2.1
LONY-Br-3	.4.8	LONY-Br-20	2.4	LONY-Br-35	1.9
LONY-Br-4	1.2	LONY-Br-21	2.4	LONY-Br-36	0.8
LONY-Br-5	0.9	LONY-Br-22	1.6	LONY-Br-37	1.0
LONY-Br-6	1.4	LONY-Br-23	1.3	LONY-Br-38	2.2
LONY-Br-7	1.3	LONY-Br-24	3.9	LONY-Br-39	1.9
LONY-Br-8	0.9	LONY-Br-25	1.9	LONY-Br-40	3.4
LONY-Br-9	6.0	LONY-Br-26	1.5	LONY-Br-41	3.9
LONY-Br-10	3.6	LONY-Br-27	1.2	LONY-Br-42	0.6
LONY-Br-11	4.6	LONY-Br-28	0.5	LONY-Br-43	1.4
LONY-Br-12	2.2	LONY-Br-29	0.6	LONY-Br-44	0.7
LONY-Br-13	1.2	LONY-Br-30	0.8	LONY-Br-45	3.0
LONY-Br-14	0.8	LONY-Br-31	0.4	LONY-Br-46	3.7
LONY-Br-15	0.9	LONY-Br-32	2.2	LONY-Br-47	0.5
LONY-Br-16	2.5	LONY-Br-33	2.6	LONY-Br-48	1.6

Example 6: Isolation of gastric and prostate clones

A stomach cancer cDNA library was established, using standard techniques, then the library was screened, using the SEREX methodology described supra, and set forth by Sahin et al., *Proc. Natl. Acad. Sci. USA* 92: 11810 (1995), and by Chen et al., *Proc. Natl. Acad. Sci. USA* 94: 1914 (1997), incorporated by reference in their entirety.

To be specific, total RNA was isolated by homogenizing tumor samples in 4M guanidium thiocyanate/0.5% sodium N-lauryl sarcosine/ and 25 mM EDTA followed by centrifugation in 5.7 M CsCl/25 mM sodium acetate/10 uM EDTA at 320,000 rpm. Total mRNA was removed by passing the sample over an oligo-dT cellulose column. The cDNA libraries were then constructed

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by taking 5 ug of mRNA, using standard methodologies to reverse transcribe the material.

Libraries were prepared from four different stomach cancer patients, referred to as "SM", "CK" and "SS" and "KM" respectively. A total of 2.5x10⁶, 1.1x10⁶, and 1.7x10⁶ cDNA clones were obtained from the "SM", "CK" and "SS" individuals. Additional libraries were prepared from prostate cancer patient "OT".

The cDNA was used to construct a lambda phage library, and 500 phages were plated onto XL1-Blue MRF E. coli, and incubated for eight hours at 37°C. A nitrocellulose membrane was then placed on the plate, followed by overnight incubation. The membrane was then washed, four times, without TBS which contained 0.05% Tween, and was then immersed in TBS containing 5% non-fat dried milk. After one hour, the membrane was incubated with conjugates of peroxidase-goat anti human IgG specific for Fc portions of huma antibody (1:2000, diluted in TBS with 1% BSA. The incubation was carried out for one hour, at room temperature, and the membrane was then washed three times with TBS. Those clones which produced antibodies were visualized with 0.06%, 3,3'diamino benzidine tetrachloride, and 0.015% H₂O₂, in 50 mM Tris (pH 7.5). Any clones which produced immunoglobulin were marked, and then the membrane was washed, two further times, with TBS that contained 0.05% Tween, and then twice with "neat" TBS.

The membranes were then incubated in 1:100 diluted patient serum, overnight, at 4°C. The patient serum had been pretreated. Specifically, 5 ml samples were diluted to 10 ml with TBS containing 1% bovine serum albumin, and 0.02% Na₃N. The serum had been treated to remove antibodies to bacteriophage, by passing it through a 5 ml Sepharose column, to which a lysate of E. coli Y1090 had been attached, followed by passage over a second column which had E. coli lysate and lysate of E. coli infected with lambda bacteriophage. The screening was carried out five time. The samples were then diluted to 50 ml, and kept at -80°C, until used as described herein.

Following the overnight incubation with the membrane, the membrane was washed twice with TBS/0.05% Tween 20, and then once with TBS. A further incubation was carried out, using the protocols discussed supra, for the POD labelled antibodies.

The positive clones were then sequenced, using standard techniques. Following comparison of the sequences to information available in data banks, a total of 36 clones were resolved into known and unknown genes. In the table that follows, the "+" and "-" signs are essentially used to compare signals to each other. All were positive. Table 5, which follows, summarizes some of this

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work isolation and sequencing of "SM" clones. Specifically, with reference to the first page of the table, previously identified human proteins and the nucleotide sequences, set forth in SEQ ID NOS:588-626 are known. The four molecules which follow in SEQ ID NOS:627-634 (gelsolin, zinc finger protein family, variant zinc finger motif protein goliath and homeodomain proteins), have not been identified in humans previously, although there are related molecules found in other species. Finally, with reference to Table 5, the last four moieties, i.e., prepro-α collagen, heterogeneous ribonucleoprotein D, nucleosome assembly protein 2, and NY-ESO-2/Ulsn NRP/V1 small nuclear ribonucleoprotein, are also known. Nucleotide sequences are set forth at SEQ ID NOS:635-642. The nucleic acid molecules having the nucleotide sequences set forth at SEQ ID NOS:643-670 represent molecules for which no related sequences were found. SEQ ID NO:671 combines the sequences of SEQ ID NOS:627-630, inclusive. SEQ ID NO:672 combines SEQ ID NOS:643-656, SEQ ID NO:673 combines SEQ ID NOS:657, 659 and 662, while SEQ ID NO:674 combines SEQ ID NOS: 658, 660, 661 and 663.

SEREX analysis of clones from libraries derived from patients "CK", "SS", "KM" (all gastric cancer) and patient "OT" (prostate cancer) was carried out as described above. The nucleotide sequences of clones derived from gastric cancer patients are presented as SEQ ID NOs:176-436. The nucleotide sequences of clones derived from prostate cancer patient "OT" are presented as SEQ ID Nos:437-543.

Example 7: Isolation and analysis of colon clones

Colon tumor samples were obtained as surgical samples, and were frozen at -80°C until ready for use.

Total RNA was then isolated from the samples, using the guanidium thiocyanate method of Chirgwin, et al., *Biochemistry* 18: 5294-5299 (1979), incorporated by reference. The total RNA thus obtained was then purified to isolate all poly A⁺ RNA, using commercially available products designed for this purpose.

The poly A⁺ RNA was then converted into cDNA, and ligated into λ ZAP, a commercially available expression vector, according to the manufacturer's suggested protocol.

Three cDNA libraries were constructed in this way, using colorectal carcinoma samples.

A fourth library, also from colorectal carcinoma, was prepared, albeit in a different way. The

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fourth library was an IgG subtraction library, prepared by using a subtraction partner, generated by PCR amplification of a cDNA clone which encoded an IgG molecule. See, e.g., Ace et al, Endocrinology 134: 1305-1309 (1994), and incorporated by reference in its entirety. IgG subtraction is done to eliminate any false, positive signals resulting from interaction of cDNA clones which encode IgG, with the IgG then interacting with the anti-human IgG used in the SEREX assay, as described herein. PCR products were biotinylated, and hybridized with denatured second strand cDNA, at 68°C for 18 hours. Biotinylated hybrid molecules were coupled to streptavidin, and then removed by phenol chloroform extraction. Any remaining cDNA was also ligated into λZAP. All libraries were amplified, prior to immunoscreening.

Immunoscreening was carried out using sera obtained from patients undergoing routine diagnostic and therapeutic procedures. The sera were stored at -70°C prior to use. Upon thawing, the sera were diluted at 1:10 in Tris buffered saline (pH 7.5), and were then passed through Sepharose 4B columns. First, the sera were passed through columns which had <u>E. coli</u> Y1090 lysates coupled thereto, and then lysates from bacteriophage infected <u>E. coli</u> BNN97 lysates. Final serum dilutions were then prepared in 0.2% non-fat dried milk/Tris buffered saline.

The method of Sahin et al., *Proc. Natl. Acad. Sci. USA* 92:11810-11813 (1995), and U.S. Patent No. 5,698,396, both of which are incorporated by reference, was used, with some modifications. Specifically, recombinant phages at a concentration of 4x10³ phages per 15 cm plate (pfus), were amplified for six hours, after which they were transferred to nitrocellulose membranes for 15 hours. The membranes then were blocked with 5% nonfat dried milk.

As an alternative to the IgG subtraction procedure discussed above, membranes were prescreened in a 1:2000 dilution of peroxidase conjugated, Fc fragment specific goat anti-human IgG, for one hour, at room temperature. Color was developed using 3,3'-diaminobenzidine tetrahydrochloride, which permitted scoring of IgG encoding clones.

Membranes were then incubated in 1:100 dilutions of autologous sera, which had been pretreated with the Sepharose 4B columns, as described <u>supra</u>. The filters were then incubated, in a 1:3000 dilution of alkaline phosphatase conjugated Fc fragment specific, goat anti-human IgG, for one hour, at room temperature. The indicator system 4-nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolyl-phosphate was then added, and color development assessed. Any positive clones were subcloned, and retested, except the time on the nitrocellulose membrane was reduced to three

Positive clones were isolated and sequenced according to standard procedures. The nucleotide sequences of the clones are set forth in the even numbered sequences from SEQ ID Nos:544-586. The odd numbered sequences from SEQ ID Nos:545-587 represent the translated amino acid sequences of the colon nucleic acid clones. Analysis of probes for SEQ ID NOS:544 and 546 confirmed their universal expression.

The foregoing results reflect SEREX isolation of colon cancer clones using autologous serum. The positive clones were then rescreened, using allogeneic serum, following the same method discussed supra, in example 2, except IgG prescreening was omitted. The allogeneic sera was obtained from sixteen normal blood donors, and twenty nine patients who had been diagnosed with colorectal cancer.

The analysis with the two types of serum revealed that fourteen reacted with a subset of sera from normal and cancer patients, twenty-eight only with autologous sera, and six with both allogeneic and autologous sera. Over 60% of the allogeneic serum samples tested reacted with at least one of these positive clones. About 20% reacted with two or more.

In view of the results described above, further experiments were carried out using serum samples from patients with other forms of cancer, i.e., renal cancer (13 samples), lung cancer (23 samples), and breast cancer (10 samples). The results are set forth in Table 6 which follows:

Table 6: Allogeneic serotyping using colon cancer clones

	Clone Number	Normal Sera	Colon Cancer	Renal Cancer	Lung Cancer	Breast Cancer
	NY-Co-8	0/16	8/29	1/13	0/23	0/10
	NY-Co-9	0/16	5/29	1/13	1/23	0/10
	NY-Co-13	0/16	5/29	0/13	0/23	0/10
	NY-Co-16	0/16	3/29	0/13	0/23	0/10
	NY-Co-20	0/16	4/29	0/13	0/23	0/10
)	NY-Co-38	0/16	4/29	3/13	0/23	1/10

Of the six clones which were identified as being reactive with autologous and allogeneic

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cancer serum, and not with normal serum, two were found to be identical to previously identified molecules (NY-Co-. Four others were found to have little or no homology to known sequences and thus are preferred allogeneic-reactive colon cancer clones. These nucleic acids and their polypeptide translations are presented as SEQ ID NOS: 544-551: SEQ ID NO: 544/545 (NY-CO-8), SEQ ID NO: 546/547 (NY-CO-9), SEQ ID NO: 548/549 (NY-CO-16) and SEQ ID NO: 550/551 (NY-CO-38). Of twenty seven allogeneic colon cancer serum samples tested, 67% reacted with at least one of these antigens.

The expression pattern of mRNA corresponding to SEQ ID NOS:544, 546 and 550, as well as other sequences identified via the preceding examples was determined. To do this, RT-PCR was carried out on a panel of RNA samples, taken from normal tissue. The panel contained RNA of lung, testis, small intestine, colon, breast, liver and placenta tissues. The RNA was purchased from a commercial source. RNA from a colon tumor sample was also included. All samples were set up for duplicate runs, so that genomic DNA contamination could be accounted for. In the controls, no reverse transcriptase was used.

Primers were designed which were specific for the cDNA, which would amplify 5'-fragments, from 300-400 base pairs in length. The PCR reactions were undertaken at an annealing temperature of 68°C. Where appropriate, 5' and 3'-RACE reactions were undertaken, using gene specific primers, and adapter primers, together with commercially available reagents. Specifically, SEQ ID NOS: 546 and 550 were tested using RACE. The resulting products were subcloned into vector pCR 2.1, screened via PCR using internal primers, and then sequenced.

SEQ ID NOS:544 and 546 were found to be amplified in all tissues tested. SEQ ID NO:550 was found in colon tumor, colon metastasis, gastric cancer, renal cancer and colon cancer cell lines Colo 204 and HT29, as well as in normal colon, small intestine, brain, stomach, testis, pancreas, liver, lung, heart, fetal brain, mammary gland, bladder, adrenal gland tissues. It is was not found in normal uterine, skeletal muscle, peripheral blood lymphocytes, placental, spleen thymus, or esophagus tissue, nor in lung cancer.

The analysis also identified differential expression of a splice variant of SEQ ID NO:550, i.e., SEQ ID NO:552. When the two sequences were compared, it was found that SEQ ID NO:550 encodes a putative protein of 652 amino acids (SEQ ID NO:551), and molecular weight of 73,337 daltons. SEQ ID NO:552, in contrast, lacks an internal 74 base pairs, corresponding to

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nucleotides 1307-1380 of SEQ ID NO:550. The deletion results in formation of a stop codon at the splice function, and a putative protein of 403 amino acids (SEQ ID NO:553), and molecular weight 45,839. The missing segment results in the putative protein lacking a PEST protein degradation sequence, thereby suggesting a longer half life for this protein.

In additional experiments, primers designed not to differentiate between SEQ ID NOS: 550 and 552 resulted in almost universal amplification (placenta being the only exception). In contrast, when primers specific for SEQ ID NO:552 were used differences were seen in normal pancreatic, liver, lung, heart, fetal brain, mammary gland, bladder, and adrenal gland tissue, where there was no expression of SEQ ID NO:552 found.

Northern blotting was also carried out for SEQ ID NOS: 544, 546, 550 and 552. These experiments employed the same commercially available RNA libraries discussed above were used.

Samples (2 ug) of polyA⁺ RNA were analyzed from these samples, using random, ³²P labelled probes 300-360 nucleotides in length, obtained from PCR products. These probes were hybridized to the RNA, for 1.5 hours, at 68°C, followed by two washes at 0.1xSSC, 0.1% SDS, 68°C, for 30 minutes each time.

SEQ ID NOs:544 and 546 were again found to be universally expressed.

Further screening identified additional isoforms of SEQ ID NOS:544 and 550. These are set forth as SEQ ID NOS: 554, 556, 558 and 560. The isoform represented by SEQ ID NO:554 (translated as SEQ ID NO:555) is a naturally occurring splice variant of SEQ ID NO:544, found in normal colon. SEQ ID NO:556 (translated as SEQ ID NO:557), which is an isoform of SEQ ID NO:550 (translated as SEQ ID NO:551), was found in brain tissue, primarily spinal chord and medulla. SEQ ID NO:558 (translated as SEQ ID NO:559), was found in normal kidney and in colon tumors, metastasized colon cancer, renal cancer, gastric cancer, and in colon cancer cell line Colo 205. It was not found in any normal tissue other than kidney.

The nucleic acid molecule whose nucleotide sequence set forth as SEQ ID NO:560 (translated as SEQ ID NO:561), is a further isoform of SEQ ID NO:552. It is similar to SEQ ID NO:558, except it contains a long nucleotide insert encoding a longer COOH terminus. It was expressed in normal bladder and kidney cells, and renal cancer cells. It was not expressed in colon cancer cells.

It is reported above that fourteen clones reacted with subsets of serum from both normal

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and cancer patients, while twenty eight reacted with autologous sera only. These clones were sequenced, in accordance with standard, art recognized methods. Of the clones which reacted only with autologous sera, nine appear to be previously unidentified sequences. These are set forth as SEQ ID NOS: 562, 564, 566, 568, 570, 572, 574, 576 and 578. SEO ID NO:562 (translated as SEQ ID NO:563) is 1445 nucleotides long, and shows some similarity to known sequences for myosin and tropomyosin. SEQ ID NO:564 (translated as SEQ ID NO:565), which is 1226 nucleotides long, contains a TPR motif. The sequence set forth in SEQ ID NO:566 (translated as SEQ ID NO:567) is 1857 nucleotides long, and shows similarity to cyclophillins. The nucleotide sequence set forth in SEQ ID NO:568 (translated as SEQ ID NO:569) is 1537 nucleotides long, and shows similarity to murine gene 22A3, which has unknown function, but resembles an unconventional form of myosin, as well as an EST for heat shock inducible mRNA. As for the molecule set forth in SEQ ID NO:570 (translated as SEQ ID NO:571), it appears to resemble a nucleic targeting signal protein. SEQ ID NO: 572 (translated as SEQ ID NO:573) is 604 nucleotides long, and may encode a lysosymal protein. The molecule set forth in SEO ID NO:574 (translated as SEQ ID NO:575) is 742 nucleotides long, and encodes a protein with an SH3 domain and which shows some similarity to GRB2 and human neutrophil oxidase factor. The molecule set forth in SEQ ID NO:576 (translated as SEQ ID NO:577) is 1087 nucleotides long, and encodes a protein which contains coiled core domains. The molecule set forth in SEO ID NO:578 (translated as SEQ ID NO:579) is 2569 nucleotides long, shows some similarity with Drosophila homeotic material tudor protein, and has a DY(F)GN repeat.

Additional sequences were identified which were expressed in both normal sera and cancer cells. The sequence set forth in SEQ ID NO:580 (translated as SEQ ID NO:581), e.g., is 2077 nucleotides long, and was expressed by both colorectal cancer and normal cells. Analysis of the sequence showed that it possesses a nuclear targeting sequence. The molecule set forth in SEQ ID NO:582 (translated as SEQ ID NO:583) is 3309 nucleotides long, was expressed by colorectal cancer and normal cells, and is similar to heat shock protein 110 family members. The molecule presented in SEQ ID NO:584 (translated as SEQ ID NO:585) was expressed in a colon to lung metastasis, as well as by normal tissue. It is 2918 nucleotides in length. Analysis shows that it contains 2 zinc finger domains. The nucleotide sequence of SEQ ID NO:586 (translated as SEQ ID NO:587) was also expressed in a colon to lung metastasis, is 1898 nucleotides long, and is

also expressed by normal tissue. Specifically, the reactivity of the molecules was as follows:

Table 7

5	SEQ ID NO:	Normal Sera Reactivity	Tumor Sera Reactivity
	580	2/16	2/16
	582	2/16	3/16
10	584	2/16	2/16
	586	2/8	1/16

A more extensive set of RT-PCR experiments were carried out to study the expression pattern of SEQ ID NOS: 550, 552, 558 and 560. The results follow.

Table 8: RT-PCR analysis of colon SEREX clones

	A more extensive set of RT-PCR experiments were carried of					
100 E	pattern of SEQ I	D NOS: 550, 552	2, 558 and 560. The results follow			
11 5	Table 8: RT-PCI	R analysis of cold	on SEREX clone	<u>es</u>		
190	normal tissue	SEQ ID NO.:550	SEQ ID NO.:552	SEQ ID NO.:558	SEQ ID NO.:560	
120 120 125	kidney colon small intest. brain stomach	+ + + + +	Negative Negative Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative Negative	
	testis pancreas lung liver	+ + + +	Negative Negative Negative Negative	Negative Negative Negative Negative	Negative Negative Negative Negative	
30	heart fetal brain mammary gland	+ + +	Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative	
35	bladder adrenal gland uterus skeletal	+ + Negative	Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative	Negative Negative Negative Negative Negative	
40	muscle PBL placenta	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative	

	spleen thymus esophagus	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative	Negative Negative Negative
	Tumor Tissue				
5	renal cancer (4) colon primary	+ (2/4)	+ (2/4)	+ (2/4)	+ (2/4)
	tumors (10)	+ (10/10)	+ (10/10)	+(10/10)	Negative
10	colon mets (4) breast	+ (4/4)	+ (4/4)	+ (4/4)	Negative
	cancer (6) lung	+ (3/6)	Negative	Negative	Negative
15	cancer (6)	+ (6/6)	Negative	Negative	Negative
	gastric cancer (1)	+	+	+	Not tested
	colon cancer cell lines				
20	colo 205 HT29 HCT15	+ + Negative	+ + Negative	+ Negative Negative	Negative Negative Negative

Example 8:Isolation and analysis of additional clones

For the establishment of a cDNA library from human tissue total RNA was obtained from 0.5 g of a renal clear cell carcinoma and established according to the method of Chomzynski as described above The mRNA was extracted from total RNA with oligo-dT-cellulose. The synthesis of the first strand cDNA was accomplished by the method described by Gubler and Hoffmann, *Gene* 25: 263 (1983) using RNase H and DNA polymerase I. For adaptation of the cDNA Klenow enzyme, adaptors with EcoRI restriction enzyme sites were ligated to the cDNA ends using T4 DNA ligase (Ferretti L and Sgamerella V, *Nucl. Acids Res.* 9: 3695 (1981)). Following restriction enzymatic digestion with the enzyme Xhol, cDNA molecules of different length were separated using Sephacryl 400 and transfected into λZAPII phage vectors (Short JM et al., *Nucleic Acids Res.* 16: 7583 (1988)). The recombinant phage DNA was packaged into phages after ligation with packaging extracts and used for the transfection of *E. coli* bacteria. The titration of the library resulted in 1.8 x 10⁶ recombinant primary clones. The total cDNA library was transfected in *E. coli* and amplified. The titer of the cDNA library after amplification was 10¹¹ plaque forming units per ml (pfu/ml). These transfected cells were used in experiments which follow.

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In accordance with the invention as described above, identification of immunogenic material was achieved by using human sera which has been completely depleted of antibodies directed against antigens derived from native and lytic λ phage-transfected E. coli bacteria. To this end, the serum was absorbed, as follows.

 $E.\ coli$ bacteria of the strain XL1-blue were cultured in 50 ml LB medium overnight. After achieving an optical density of $OD_{600} = 1.0$, the bacteria were pelleted by centrifugation, resuspended in 5 ml phosphate buffered saline (PBS), and lysed by sonication. The bacterial lysate was bound onto a matrix of activated Sepharose, which was then put into a column and used for the absorption of the human serum. The serum was run over this column 10 times.

A culture of $E.\ coli$ XL1 blue bacteria in the exponential growth phase was pelleted by centrifugation, transfected in 0.01 M magnesium sulfate with $10^6\ \lambda ZAPII$ phages without a recombinant insert and incubated in 5 ml LB medium for four hours. The lysate of the transfected bacteria was used in the same manner as the untransfected bacteria, with the human serum described supra being passed through the column an addition ten times.

To complete the depletion of the serum, interfering antibodies from lytically transfected *E. coli* bacteria were cultured on agar plates and their proteins were blotted onto nitrocellulose membranes after 10 hours of culture at 37°C. Following this, the serum which had been preabsorbed according to the above steps was transferred to the blotted nitrocellulose membrane, and the absorption procedure was repeated five times. The serum, which was processed in accordance with the invention, was totally depleted of antibodies directed against antigens derived from *E. coli* and phages.

In this, a renal cancer-specific antigen was identified via the following steps. Bacteria of the strain XL1 blue were transfected with recombinant phages derived from the described cDNA library and plated at a density of 4-5x10³ plaque forming units (pfu) per plate in LB-medium with isopropylthiogalactopyranoside ("IPTG"). After 12 hours of incubation at 37°C, nitrocellulose membranes were put on top of the cultures and culture plates were incubated for another four hours. This was followed by incubation of the nitrocellulose membrane for one hour in Tris-buffered saline (PBS) with 5% milk powder. After washing the nitrocellulose membranes three times in TBS, the stripped human serum secured following Example 2 was diluted 1:1000 in TBS/0.5% (w/v) milk power and incubated overnight with gentle shaking. After the incubation with the nitrocellulose

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membrane the serum was removed and kept for additional testing. Following incubation with serum, the nitrocellulose membranes were washed three times in TBS, and incubated with a polyclonal alkaline phosphatase-conjugated goat anti-human IgG serum for one hour. Following this, the nitrocellulose membranes were washed repeatedly with TBS/0.01% (v/v Tween 20). The reaction was developed using nitroblue tetrazolium chloride and bromochloro-indoyl-phosphate in TBS. The binding of human antibodies to the expressed protein became visible by a blue ringformed color deposit on the nitro-cellulose membrane. The efficient preabsorption of the serum made in possible to develop the membrane at 37°C over several hours without compromising the quality of the test because of background reactivity caused by antibodies against *E. coli* and phage antigens.

Positive clones were localized on the agar plates, transferred into transfection buffer, and used for a second round of transfection and subcloning. A total of 1.8x10⁶ recombinant clones were subjected to screening and five different positive-reacting clones were identified.

Positive clones, i.e., those which had bound antibodies derived from the processed human serum, were subcloned to monoclonality by repeated rounds of transfection and testing of reactivity with the processed human serum. P-bluescript phagemids with the respective cDNA inserts were cloned by in vivo excision (Hay B and Short JM, Strategies 5: 16-19, 1992) from the λZAPII phage vectors and used for the transfection of E. coli SOLR bacteria. Plasmids were isolated from the bacteria after alkaline lysis with NaOH in a modification of the method of Birnboim HC and Doly J. J. Nucl. Acids Res. 7: 1513 (1979). The recombinant plasmid DNA was sequenced according to standard methods using M13-forward and M13-reverse oligonucleotides. The DNA sequence obtained and the resulting amino acid sequence were compared with nucleic acid and protein data banks (Gene Bank, EMBL, Swiss Prot). The sequencing of the cDNA inserts was continued using internal oligonucleotides. Analysis showed no homology with any sequences deposited in the data banks. The full length cDNA clone, referred to as SK313, was cloned with the RACE method (Frohman MA, Dush MK, Martin GR, Proc. Natl. Acad Sci. USA 85: 8998 (1988)), and had a carbonic anhydrase domain at the 5' end.

As a continuation of these experiments, RNA was isolated from a spectrum of malignant and normal human tissues and Northern blots were performed with labeled SK313 (also referred to as clone HOM-RCC-313). The Norther blot analysis demonstrated that the mRNA of clone HOM-

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RCC-313 was overexpressed in 4 out of 19 renal cell carcinomas compared to normal kidneys. Very weak expression was found only in colonic mucosal tissue and in normal kidney. Expression in other tissues was not observed.

To determine the incidence of antibodies against antigens which are identified above, allogeneic sera from healthy individuals and tumor patients were analyzed. To this end, the sera were processed as described above and depleted from antibodies against antigens derived from *E. coli* and phages. For the detection of antigen-specific antibodies, phages derived from reactive clones were mixed with non-reactive phages derived from the same cDNA library at a ratio of 1:10 and tested as described above for reactivity with antibodies in the human test serum. The serum which had been used for the identification of the antigen was used as a positive control. The non-reactive phages served as a negative control. A serum sample was positive for antigen reactive antibodies, if the expected percentage of the phage plaques showed a positive reaction. In the case of the renal cell carcinoma antigen represented by clone HOM-RCC-313, the analysis of a spectrum of human sera showed that only sera from renal cell carcinoma patients contained reactive antibodies. Sera from healthy controls and patients with other tumors did not contain such antibodies.

The cDNA for clone HOM-RCC-313 was excised from the plasmid DNA by digestion with the restriction enzyme EcoR1, was separated by agarose gel electrophoresis, followed by extraction from the gel. This was then used to create a vector which expresses a fusion protein with the bacterial protein anthranilate synthetase. A relevant fragment in the exact open reading frame was cloned into pATH plasmid vectors (Koerner et al., *Meth. Enzymol.* 194: 477 (1991)). Induction of protein expression was obtained after transformation of the plasmids into E. coli of strain BL21 as described (Spindleret al., *J. Virol.* 49: 132 (1984)). Expressed fusion proteins were separated by SDS gel electrophoresis, excised from the gel, eluted and freeze dried. Rabbits were immunized by subcutaneous injection with 100 µg of the lyophilisate combined with Freund's adjuvant according to standard procedures. Immunization was repeated three times at two-week intervals using incomplete Freund's adjuvant. The rabbit was bled and antiserum was obtained. The obtained antiserum was depleted from antibodies reactive with E. coli and phages as described above and tested for reactivity against the renal carcinoma antigen as described for the human serum.

30 Reactivity was detected at dilutions of 1: >100,000.

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Additional clones were identified from pancreatic cancer tumor specimen using the SEREX method of Sahin et al., (1995). A cDNA library was prepared and reacted with high titer IgG in sera of pancreatic carcinoma patients. A total of 8x10⁵ clones were screened with autologous serum, and 4.5x10³ clones were screened with three different allogeneic sera. Twenty three clones, representing seven different transcripts were found. Four were previously unknown, unisolated genes. Of the remaining three, glycolytic enzyme aldolase A was found (SEQ ID Nos:799 and 800). Another molecule was "known" in that it was homologous to the rat eIF-5 gene (SEQ ID Nos:801 and 802), which is a eukaryotic translation initiation factor. The human eIF-5 gene was not previously known.

When hepatocelullar carcinoma libraries were studied in the same way, a total of 1.5x10⁶ clones were screened, and 98 positives were found. A total of 59 of these were sequenced, and corresponded to at least 20 different transcripts. Nine of these were assayed with allogeneic sera from hepatocellular cancer (HCC) patients and normal patients. High titered antibody was restricted to HCC patients. The majority of isolated sequences did not correspond to known molecules. Three which did were human albumin (SEQ ID Nos:803 and 804), senescence marker protein SMP30 (SEQ ID NOs:805 and 806), and C3VS (SEQ ID NOs:807 and 808). The latter was overexpressed in 2 of 4 hepatocarcinoma tissues, as compared to normal. Expression of SMP30 was found to vary highly.

The methodology was combined with subtractive cDNA techniques when assaying leukemia cells (T-ALL). An antigen was found which was identical to a broadly expressed, DNA repair enzyme.

Further assays identified the known molecule galectin-9 (SEQ ID NOs:809 and 810), as being highly expressed on human macrophages and dendritic cells. Expression is upregulated during differentiation of monocytes to macrophages. Highest levels were found on monocyte derived, dendritic cells.

Fusion proteins "LD1-mFc" and "LD2-mFc" were constructed to help analyze galectin-9. These consist of murine IgG heavy chain fragments, and a lectin domain (LD1, or LD2), as the N-terminus. Analysis indicated that the C-terminal lectin domain binds to the surface ligands, while the cell surface ligands recognized by the C-terminal lectin domain of galactin-9 was expressed only in a small, subpopulation of dendritic cells.

Further analysis of ovarian cancer cells (500,000 clones, using the SEREX method described

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above), identified previously known antigens MAGE-4 (SEQ ID Nos:811 and 812) and restin (SEQ ID Nos:813 and 814), and six other newly identified molecules.

Further experiments were carried out which involved restin. A variation of restin is known, i.e., "CLIP170", which was reported to mediate binding of endosomes to microlubules. It was found that both resin and CLIP 170 are highly expressed in dendritic cells, and are involved in the formation and transport of macropinosomes, a feature of professional antigen presenting cells. Expression of restin was induced after 48 hours of culture of monocytes in GM-CSF/IL-4 supplemented medium. Highest levels were found in immature dendritic cells. When microlubile systems, which are essential for the activity of restin/CLIP-170 were disrupted, macropinocytosis was lost completely.

Further work with the methodology disclosed herein on glioma identified a clone encoding nm23-H2 protein (SEQ ID Nos:815 and 816). This clone corresponds to subunit B of nucleoside diphosphate kinase, which is implicated in tumor metastasis control. It is also known as PuF, a transcriptional factor, for c-myc proto-oncogenes. Antibodies against the protein were found in 1 of 18 sera of brain malignancy patients, 3 of 20 melanoma patients, and 2 of 20 sera from healthy patients. When expression studies were carried out using RT-PCR, 25 of 28 brain tumor, and 4 or 5 mengioma tumor samples were found to express the gene.

Example 9:Isolation and analysis of lung cancer clones

A cDNA library was constructed from a case of moderately differentiated adenocarcinoma of the lung, obtained from the Department of Pathology at The New York Hospital. The library was constructed in a λZAP Express vector using a cDNA library kit (Stratagene, La Jolla, CA).

The cDNA library was screened with autologous patient's serum as described previously [Sahin, U. et al., *Proc Natl Acad Sci USA* 92:11810-3 (1995); Chen, Y.T. et al. *Proc Natl Acad Sci USA*. 94:1914-8 (1997)]. Briefly, the serum was diluted 1:10, pre-absorbed with transfected *E. coli* lysate, and a 1:10 dilution of the absorbed serum (final dilution of serum 1:100) was incubated overnight at room temperature with the nitrocellulose membranes containing the phage plaques. After washing, the filters were incubated with alkaline phosphatase-conjugated goat anti-human Fc γ secondary antibodies and the reactive phage plaques were visualized by incubating with 5-bromo-4-chloro-3-indolyl-phosphate and nitroblue tetrazolium. Phagemid clones encoding human

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immunoglobulin sequences were subsequently eliminated during the secondary screening.

The reactive clones were subcloned, purified, and *in vitro* excised to pBK-CMV plasmid forms (Stratagene). Plasmid DNA was prepared using Wizard Miniprep DNA Purification System (Promega, Madison, WI). The inserted DNA was evaluated by EcoRI-XbaI restriction mapping, and clones representing different cDNA inserts were sequenced. The sequencing reactions were performed by DNA Services at Cornell University (Ithaca, NY) using ABI PRISM (Perkin Elmer) automated sequencers.

To evaluate the mRNA expression pattern of the cloned cDNA in normal and malignant tissues, gene-specific oligonucleotide primers for PCR were designed to amplify cDNA segments of 300-400bp in length, with the estimated primer melting temperature in the range of 65-70°C. All primers were commercially synthesized (Operon Technologies, Alameda, CA). RT-PCR were performed using 35 amplification cycles in a thermal cycler (Perkin Elmer) at an annealing temperature of 60°C.

Genomic DNA were extracted from cell lines and frozen tumor tissue. Following restriction enzyme digestion, the DNA was separated on a 0.7% agarose gel, blotted onto nitrocellulose filters, and hybridized to an a ³²P-labeled DNA probe at high stringency (65°C, aqueous buffer). Washing of the blot was also under high stringency conditions, with a final wash in 0.2XSSC with 0.2% SDS at 65°C.

To identify the 5'end of the mRNA transcripts, RACE (rapid amplification of cDNA ends) methodology was utilized using the Marathon cDNA amplification kit (Clontech) and adaptor-ligated testicular cDNA as the substrate. The PCR products, after separation by agarose gel electrophoresis, were cloned into the direct PCR cloning vector pGEM-T (Promega).

Single-strand conformation polymorphism (SSCP) analysis was performed to analyze cDNA from various tissues, using previously described protocols [Dracopoli, C.D. et al., New York: John Wiley and Sons, Inc. (1997)]. Briefly, PCR was performed with 5 μ l RT product in a final volume of 25 μ l, with 2 μ Ci of α^{32} P-dCTP (~3000 Ci/mmole, New England Nuclear) per reaction. The PCR conditions was as described for RT-PCR above. After the PCR, 1 μ l of the mixture was diluted with 5 μ l of denaturing buffer (95% formamide, 20 mM EDTA, 0.05% bromophenol blue, 0.05% xylene cyanol), heat-denatured at 98°C for 2 min, and electrophoresed through an 8% polyacrylamide gel with 10% glycerol. As controls, aliquots of the same samples were diluted with a standard non-

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denaturing DNA loading dye and electrophoresed in parallel. The electrophoresis was performed at room temperature at a constant power of 10-12 watts. The gel was then dried and autoradiography performed for 15-24 hours with an intensifying screen.

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Identification of Immunoreactive cDNA clones

A cDNA expression library of 1.42x10⁷ primary clones was prepared from Lu15, a specimen of moderately differentiated adenocarcinoma of the lung and 8x10⁵ phage plaques were immunoscreened with absorbed autologous patient serum at 1:100 dilution. Excluding false-positive clones encoding immunoglobulin gene fragments, 20 positive clones were identified. These clones were purified and sequence analyzed. Comparisons of the sequences showed that these clones represented cDNAs from 12 distinct genes, designated NY-LU-1 through NY-LU-12 (Table 9). A homology search through the GenBank/EMBO databases revealed that 4 of the 12 genes corresponded to previously known molecules, and 8 others were unknown genes, with sequence identity limited only to short segments of known genes or to expressed sequence tags (ESTs).

Table 9: NY-LU clones

Gene Designation	Gene/Sequence Identity [Accession Number]	cDNA	Comments
NY-LU-1	Aldolase A (N and H type) [X06352]	Lu-15/24, 72, 83, 158, 219, 241	Human fructose, 1,6 diphosphate aldolase A. Expressed in muscle (M type), but also in most other tissues (N and H types). Levels increased in most lung cancers; released into blood upon trauma and in several cancers.
NY-LU-2	hASNA-1 [U60276]	Lu-15/26, 66	Human homolog of the ATP-biding ars A component of the bacterial arsenite transporter. Previously cloned by SEREX from a testicular library (Chen et al., unpolished). Ubiquitously expressed.
NY-LU-3	Annexin 1X [L19605]	LU-15/64	Homosapiens 56K autoantigen. Antibodies to Annexin 1X are found in multiple autoimmune diseases. ubiquitously expressed.

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NY-LU-4	Rip-1	Lu-15/65	Human HIV Rev-interacting protein. Expressed
	[U55766]		in B cells, monocytes and rhabdomyoma cells.
NY-LU-5	Unknown	Lu-15/80	Expressed ubiquitously (by RT-PCR).
	[W61291, W92962, etc.]		
NY-LU-6	Unknown	Lu-15/85	Sequence contains no ORF, expressed
	[none]		ubiquitously (by RT-PCR).
NY-LU-7	Unknown	Lu-	Expressed in neuron, pregnant uterus, lung ca.,
	[W23466, AA167732,	15/135,217	parathyroid tumors, etc.
	etc.]		
NY-LU-8	Unknown	Lu-15/139	Expressed in fetal heart, retin, multiple sclerosis,
	[Z78323, N39225, etc.]		etc.
NY-LU-9	Unknown	Lu-15/145	Expressed in retina, pregnant uterus, fetal liver-
	[W26569, AA036884,		spleen, etc.
	etc.]		
NY-LU-10	Unknown	Lu-15/154	Expressed in colon, pancreas, pregnant uterus,
	[M29204, etc.]		fibroblasts, etc.
NY-LU-11	Unknown	Lu-15/270	Expressed in retina, pregnant uterus, fetal heart,
	[W23466, AA057400,		fetal liver-spleen, parathyroid tumors, etc.
	etc.]		
NY-LU-12	g16	Lu-15/251	Located at the 3p21 TSG locus (see text)

Of the 4 known genes, aldolase A (NY-LU-1; SEQ ID NOs:689 and 690) was most frequently isolated, representing 6 of 20 primary positive clones in the entire screening. NY-LU-2 (SEQ ID NO:691), represented by two isolates, was the human homolog of the ATP-binding arsA component of the bacterial arsenite transporter, a gene which has been shown to be ubiquitously expressed in various tissues [Kurdi-Haidar, B. et al., *Genomics* 36:486-91 (1996)]. NY-LU-3 (SEQ ID Nos:692 and 693) encodes annexin XI, which is a 56KD ubiquitously expressed antigen to which autoantibodies have been described in sera from patients with various autoimmune diseases [Misaki, Y. et al., *J Biol Chem* 269:4240-6 (1994); Misaki, Y. et al., *J Rheumatol*. 22:97-102 (1995)]. The last gene in this group, NY-LU-4 (SEQ ID NOs:694 and 695), codes for the human HIV Rev interacting protein Rip-1, which has been shown to be expressed in the monocyte cell line U937, the rhabdomyoma cell line RD, as well as in adherent monocytes and primary lymphocytes [Refaeli, Y.

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et al., Proc Natl Acad Sci USA 92:3621-5 (1995)].

Of the eight unknown genes, 6 (NY-LU-5, 7, 8, 9, 10, 11; SEQ ID Nos:696, 698, 699, 700, 701 and 702/703, respectively) shared sequence identify with reported expressed sequence tags (EST), likely representing cDNA products derived from the same genes. These ESTs were derived from various somatic tissues unrelated to lung, e.g., neuron, pregnant uterus, colon, endothelial cells, etc., suggesting that these genes are widely expressed in human tissues (Table 9), making them unlikely candidates for vaccine-based tumor immunotherapy. These clones were not further investigated. The only novel gene in this group, NY-LU-6 (SEQ ID NO:697), showed no sequence identity to deposited sequences in the public databases. The tissue expression pattern of this gene was evaluated by RT-PCR analysis using gene-specific primers and a normal tissue RNA panel consisting of lung, colon, kidney, liver, brain and testis. Results showed universal expression in these tissues, and this clone was not further analyzed.

NY-LU-12 is on TSG locus of chromosome 3p21.

The last gene in the unknown gene group, NY-LU-12, was represented by the immunoreactive clone Lu15-251. This clone, 1081bp in length, contained an uninterrupted open reading frame (ORF) of 952 bp, followed by a 129bp 3'untranslated region. No translation initiation codon was identified, indicating that this was a partial cDNA clone.

A sequence homology search revealed that this gene shared up to 30% homology with two different human proteins at its C-terminus (Fig. 1), LUCA15 and DXS8237E (GenBank accession numbers U23946, and P98175) and also shared homology to S1-1, the rat counterpart of DXS8237E [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)]. LUCA15 was subsequently proven to be a gene immediately centromeric to NY-LU-12 on the *TSG* locus on chromosome 3p21 (see below and [Wei, M.H. et al., *Cancer Res.* 56: 2487-92 (1996))]. Our analysis of LUCA15 revealed the presence of a nuclear localization signal in the putative LUCA15 protein. DXS8237E, was located on chromosome Xp11.23 [Coleman, M.P. et al., *Genomics* 31:135-8 (1996)] and its rat homolog, S1-1, has been shown to be an RNA-binding protein [Inoue, A. et al., *Nucleic Acids Res.* 24:2990-7 (1996)].

Of particular interest, however, was that a short segment (92bp) at the 5' end of NY-LU-12 was identical to a previously identified gene, g16 (GenBank accession number U50839), which was

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mapped to chromosome 3p21.3 and was interrupted in the small cell lung cancer line NCI-H740.

To compare NY-LU-12 with g16, the full-length NY-LU-12 cDNA sequence was obtained from normal testicular mRNA through a combination of 5'RACE and direct PCR cloning strategies. The predominant cDNA form (SEQ ID No:707), excluding the poly A tail, is of 3591bp in length. An open-reading-frame of 1123 amino acid residues (SEQ ID No:708) was identified (nt. 102-3470), with 101bp of 5' untranslated and 129bp of the 3' untranslated region. The nucleotide and amino acid sequences are shown in Fig. 2.

Comparison with the g16 sequence verified that these two are identical genes and mapped NY-LU-12 to *TSG* locus on 3p21. However, the reported g16 sequence, 2433 bp in length, lacks the 5' end 110 bases which include the translational initiation codon at nucleotide 102, and also the 3' end 980 nucleotides of NY-LU-12. In addition, 74bp DNA segment (nt. 1587-1659 of NY-LU-12) was absent in the reported g16 sequence. Oligonucleotide primers flanking this 74 bp region were designed and used to amplify RNA from 1 normal lung, 5 lung cancer cell lines, and 6 lung cancer specimens. Two RT-PCR products were seen in every specimen, corresponding to the sizes of the two cDNA variants. It was thus concluded that this variation represents an alternate splicing event which occurs in both normal and cancerous lung tissues. Of interest, however, was the difference in the putative translational products resulting from this additional 74bp exon. In the absence of this exon, the open-reading-frame of NY-LU-12 would end in the termination codon at nt.1736, as reported for g16, with a total length of 520 amino acid residues (in contrast to 1123 residues in the longer transcript). Moreover, this shorter form would not encode the C-terminal portion of the NY-LU-12 protein, the segment responsible for the immunoreactivity of Lu15-251 to the autologous patient serum.

Additional cDNA variants of NY-LU-12

In the process of 5'RACE cloning of the full-length NY-LU-12, three minor forms of cDNA products were identified which varied in their transcriptional initiation site and in their exon usage in the 5' segment of this gene. These variants will be described as transcripts B, C, and D (SEQ ID Nos:709, 711 and 712). Fig. 3 shows the comparison of these transcripts to the predominant cDNA form (transcript A, see Fig. 2).

Transcript B (Fig. 3A, bottom) contains an additional exon of 208 base pairs, inserted at

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nucleotide 145 of the NY-LU-12 sequence. The original ORF of NY-LU-12 is disrupted due to this inserted sequence, and the AUG initiation codon used by transcript A is thus unlikely to be used by this transcript. A new potential translational initiation site, however, is found within this new exon and would continue the translation into the ORF of transcript A. The final product would be a protein of 1177 amino acids (SEQ ID NO:710), with the 69 residues at the N-terminus different from transcript A. Interestingly, this new exon encodes for a signal peptide not present in the transcript A (Fig. 3A, bottom), and it is possible that these two products are localized to different subcellular compartments.

Similar to transcript B, transcripts C and D both contained additional exon(s) not present in transcript A. Transcript C contained two extra exons in tandem and a length of 364bp, only one of which (137bp) was present in transcript D, Figure 3B. These extra exon(s), inserted at the same alternate splicing site as transcript B, disrupted the original ORF, and the only long ORF would initiate at nucleotide position 498 of NY-LU-12 (959 of transcript C, 635 of transcript D). Considering the long untranslated region at the 5' end, it is doubtful whether transcripts C and D are indeed translated *in vivo*.

Correlating with this variation of NY-LU-12 mRNA, Northern blot analysis showed several RNA species in normal tissues, ranging approximately from 3 to 4.4 Kb. The intensity of individual bands also appear to vary among different tissues, suggesting post-transcriptional tissue specific regulation of NY-LU-12 mRNA.

Features of NY-LU-12 and its putative gene product

Analysis of the NY-LU-12 amino acid sequence showed 20 inexact 6 amino acid repeats with a consensus sequence of D(F/Y)RGR(D/E) close to the N-terminus (Fig. 2). These repeats were separated by 4 to 6 amino acid intervals, which showed no apparent sequence homology among each other. This feature in primary sequence is distinctive among known proteins. Hydrophilicity plot revealed that this region, although hydrophilic in general, has regular hydrophobic turns, and these cycles of hydrophilicity changes correspond to the hexapeptide repeats. Although the significance of this characteristic is unclear at present, this segment of sequence is highly rich in arginine and aspartic acid, a feature shared by RNA binding proteins. Similar motifs, rich in arginine and aspartic acid residues, were found in other RNA-binding proteins [Witte, M.M.

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et al., *Proc Natl Acad Sci USA* 94: 1212-7 (1997); Wilson, R. et al., *Nature* 368:32-8 (1994); Seraphin, B. et al., *Nature* 337:84-7 (1989); Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], e.g., RNA [Seraphin, B. et al., *Nature* 337:84-7 (1989)] hnRNA 3'end cleavage stimulation factor [Takagaki, Y. et al., *Proc Natl Acad Sci USA* 89:1403-7 (1992)], etc., indicating that NY-LU-12 is likely to be an RNA-binding protein. Consistent with this, PROSITE analysis of the putative NY-LU-12 protein identified a bipartite nuclear localization signal between amino acids 1016-1032 and a 4-residue nuclear localization pattern (PRKR) at amino acid 604-607 (Fig. 2), suggesting that NY-LU-12 is a nuclear protein. Analysis for post-translational modification sites showed potential sites for tyrosine sulfation, amidation, as well as phosphorylation sites for protein kinase A, C, casein kinase II, and tyrosine kinase. A PEST region, peptide sequences consistently found among unstable proteins with short half lives, was identified at amino acids 897-928 (Fig. 2), implying NY-LU-12 as an unstable protein.

Southern blot analysis of NY-LU-12 in normal and tumor tissues

To investigate the status of NY-LU-12 in normal and tumor cells, Southern blot analysis was performed on 9 lung cancer cell lines (3 adenocarcinoma, 2 squamous, and 3 large cell anaplastic), Lu15 tumor DNA, and a colon cancer cell line HT29 (Fig. 4). (HT29 was included due to the finding of an EST identified in the GenBank, accession number AA079461, which appeared to be a fusion sequence between semaphorin IV gene and NY-LU-12.) Using a 1.1Kb cDNA probe (nucleotide 1095-2140) and HindIII digested DNA, the results showed that one of the two hybridizing bands was absent in NCI-H740, confirming that NY-LU-12 was partially deleted in this cell line. The breakpoint of this deletion, by using primers from different regions, was further defined to be between nucleotides 1433 and 1777 of NY-LU-12, with the 3' sequences homozygously deleted. Besides NCI-H740, however, no evidence of homozygous deletion was seen in any other tumor cell line sample or in LU15. The similar band intensities and identical sizes of the DNA signals in all specimens also argued against the possibility of a heterozygous deletion or translocation of this gene, at least in the region analyzed. No change was found in HT29, suggesting that the semaphorin IV/NY-LU-12 fusion sequence in the GenBank probably represents a cloning artifact.

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SSCP and sequence analysis of NY-LU-12 in Lu15 tumor DNA.

The mapping of NY-LU-12 to the lung cancer *TSG* locus raised the possibility that an altered protein product due to mutational event may be the basis for the autologous immune recognition. This possibility was explored using DNA sequencing and single-strand confirmational polymorphism (SSCP) analysis.

The DNA sequence contained in the immunoreactive clone Lu15-251 (nucleotide 2518-3599 of NY-LU-12) was obtained from the normal counterpart by RT-PCR cloning using autologous normal lung tissue, and no mutations were found when compared to Lu15-251.

RT-PCR SSCP was then used to analyze the entire NY-LU-12 gene, comparing Lu15 tumor tissue and autologous normal lung tissue. To encompass the whole sequence, 10 sets of primer pairs were designed, each amplifying a range of 205 to 603 bps. For products >400bps, a restriction enzyme digestion step was added prior to the electrophoresis step to further reduce the fragment sizes and increase the assay sensitivity. Results showed no reproducible changes between normal and tumor tissues, and thus no evidence of mutation in Lu15 tumor cDNA. A representative set of SSCP analysis is shown in Fig. 5.

Serological response to NY-LU-12 in lung cancer patient

The frequency of anti-NY-LU-12 response was examined among normal adult and patient sera using the phage plaque assay identical to the original immunoscreening procedure. Of 21 absorbed sera from allogeneic lung cancer patients, one (Lu22) reacted strongly with the Lu15-251 plaque at 1:1000 dilution, and another (Lu7) also reacted at 1:1000, but only weakly. Nineteen other lung cancer patient sera were non-reactive, nor were the sera from 16 healthy donors, 15 colon cancer, 5 breast cancer, 1 renal cancer, 1 prostate cancer, 1 esophageal cancer, and 1 melanoma patients.

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Example 10: Expression analysis of additional cancer associated nucleic acids

The clone RING 3 was isolated from breast SEREX analysis as LONY-Br-5 (see above). The gene was identified as homologous to the "bromodomain testis" gene (BRDT; GenBank accession number AF019085). Analysis of related genes identified BRDT as a gene expressed only in testis, which was then investigated by RT-PCR analysis as described above.

The primers used to perform RT-PCR had the following sequences:

BRDT F1: CAAGAAAGGCACTCAACAG (bp 543-563 of BRDT)

BRDT R1: TTCACTACTTGCTTTAACTGC (bp 776-797 of BRDT)

The meiotic protein H1T (Histone 1 Testis; GenBank accession number M60094) was

5 identified through a literature search for meiotic proteins (testis specific expression).

The primers used to perform RT-PCR had the following sequences:

H1F1: TGCCGAACCTCTCTGTGTC (bp 116-135 of H1T)

H1R1: GCTTCGTGTAGATTTAGGAATC (bp 344-366 of H1T)

10 Table 10: RT-PCR analysis

	Normal Tissue	<u>BRDT</u>	<u>H1T</u>
1			
15 15 15	mammary gland	-	-
	liver	-	-
15	small intestine	-	-
.n	brain	-	+/- (very weak)
i E	lung	-	-
ıŌ	fetal brain	-	-
H	placenta	+	+
20 1	kidney	-	-
in.	skeletal muscle	-	-
land Nati	pancreas	-	-
1785 1785	adrenal gland	-	-
1	heart	-	-
25	thymus	-	-
	uterus	-	-
	prostate	-	+/- (very weak)
	spleen		•
	Testis	+	+
30			
	Tumor Tissue	<u>BRDT</u>	<u>H1T</u>
	Colon	0/6	0/6
35	Breast	0/6	6/6+
	Melanoma	0/12	3/12+
	Lung	8/26+	4/26+
	Renal	0/2	0/2
	Ovary	0/2	0/2
40	Esophageal	0/1	0/1

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Gastric 0/1 0/1 Bladder 0/2 0/2

Lung cancer specific expression of BRDT was observed (see table above). BRDT was expressed only in normal testis and possibly in placenta. The expression analysis of H1T revealed that all breast tumor samples (6 of 6) and ~30% lung cancers and melanoma tissue samples expressed H1T. H1T was expressed in normal testis and possibly in placenta and brain.

Example 11: allogeneic serotyping

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To confirm the cancer associated expression of SEREX clones, allogenic sera screening of gastric cancer patients' sera was conducted. Sera from normal patients (gastritis) was used as a control for expression of the clones in non-gastric cancer. The screening procedure used was as described above for the SEREX screening, except for the absorption of anti-bacterial and anti-bacteriophage antibodies. The modifications were as follows.

Serum from a stomach cancer patient or a normal individual was diluted to 1:10 in TBS (Tris buffered saline; final volume 5 ml) and passed through a column (BIO-RAD Poly-Prep Chromatography Column, Hercules. CA, USA) containing 0.5 ml Sepharose-4B cross linked to E. coli Y1090 lysate and 0.5 ml Sepharose-4B cross linked to E. coli BNN97 (5 Prime 3 Prime, Inc, Boulder, CO, USA). After repeating the column chromatography 10 times, serum was then diluted to 1:100 in TBS containing 1% BSA and 0.02% sodium azide. To remove antibodies to bacteria and baceteriophages further, 10 ml absorbed serum was incubated overnight with a 82 mm nitrocellulose membrane on which XL-1 Blue MRF' bacteria and lambda ZAP Express phages (Stratagene, La Jolla, CA USA) were immobilized. The serum was stored at - 80°C until use. For allogeneic typing, an equal numbers of positive phage and negative phage were mixed and plated and processed by the standard SEREX screening procedure.

The results of the allogenic screening experiments follow:

Table 11: Allogenic Sera Screening of SEREX Sequences from Gastric Patients

Sequence		Isolated	Allogenic Serotyping	Allogenic Serotyping
a .a.		in Serex	Gastric Cancer Sera	Normal Sera
Gene/Clone	Number	Patients		
RPB-J H-2K binding factor		SM1	6/12	6/16
Telomeric repeat binding protein		SM1 ·	1/12	0/16
Ser/Thr protein kinase		SM1	1/12	0/16
SRY interacting protein-1		SM1	2/12	1/16
Sterol carrier protein X		SM1	2/12	0/16
Archain		SM1	1/12	1/16
HEM-1		SM1	2/12	1/16
Id-1 helix-loop-helix protein		SM1	1/12	0/16
helix-loop-helix transcription factor		SM1	1/12	0/16
Follistatin related precursor protein		SM1,CK, KM	6/12	0/16
Translation initiation factor eIF-4gamma		SM1,SS1, KM	5/12	2/16
M phase phophoprotein I		SM1,SS1	8/12	5/16
Lysal tRNA synthase		SM1	1/12	0/16
Gelsolin		SM1	4/12	0/16
Zinc finger protein		SM1	1/12	1/16
Goliath		SM1	2/12	1/16
zhx-1		SM1	1/12	1/16
SG24		SM1,SS1, KM	5/12	0/16
SG132		SMI	3/12	0/16
S553		SM1	7/12	7/16
S134		SM1	3/12	0/16
S328		SM1	2/12	1/16
S365		SM1, KM	2/12	0/16

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FKBP25	KM, SS1	5/12	0/16
Pros-27	KM, CK	3/12	1/16
BS4	KM	1/12	1/16
GnRH-II	KM	1/12	0/16
CTBP	KM	1/12	0/16
ETF	KM	3/12	1/16
KIAA0438	KM	1/12	5/16
KIAA0367	KM	4/12	3/16
APK1	KM	2/12	0/16
IPP	КМ	1/12	0/16
Tropomyosin	KM	1/12	0/16
p63	КМ	1/12	0/16
KIAA0181	КМ	1/12	0/16
KIAA0349	KM	1/12	0/16
RPB1	КМ	5/12	9/15
PPIM	KM	1/12	-
EB virus	KM	3/12	-
G.KM073	KM	6/12	-
G.KM403	KM	1/12	-
KM192	KM	1/12	-
KM294	KM	1/12	-
KM362	KM	1/12	-
KM031	KM	1/12	-
KM081	KM	3/12	-
KM201	КМ	1/12	-
KM1496	КМ	1/12	-
KM334	KM	1/12	-
KM313	КМ	1/12	
E-cad/Y	CK	1/12	0/16
IPBP	SS1	1/4	-
OS-9	SS1	1/4	-

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Kinesin light chain	SS1	1/4	_
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The screening results shown above confirm the association of the SEREX clones with cancer. There is a higher correlation of cancer and the expression of certain clones, in particular, follistatin related precursor protein, the translation initiation factor eIF-4gamma, the unknown sequence SG24, the FK506-binding protein 25, and the unknown sequence G.KM073. These clones are well suited to serve as diagnostic indicators of disease and as targets for therapeutics (e.g., vaccine compositions) development.

10 Example 12: Preparation of recombinant cancer associated antigens

To facilitate screening of patients' sera for antibodies reactive with cancer associated antigens, for example by ELISA, recombinant proteins are prepared according to standard procedures. In one method, the clones encoding cancer associated antigens are subcloned into a baculovirus expression vector, and the recombinant expression vectors are introduced into appropriate insect cells. Baculovirus/insect cloning systems are preferred because post-translational modifications are carried out in the insect cells. Another preferred eukaryotic system is the *Drosophila* Expression System from Invitrogen. Clones which express high amounts of the recombinant protein are selected and used to produce the recombinant proteins. The recombinant proteins are tested for antibody recognition using serum from the patient which was used to isolated the particular clone, or in the case of cancer associated antigens recognized by allogeneic sera, e.g. certain breast cancer and gastric cancer associated antigens, by the sera from any of the patients used to isolate the clones or sera which recognize the clones' gene products.

Alternatively, the cancer associated antigen clones are inserted into a prokaryotic expression vector for production of recombinant proteins in bacteria. Other systems, including yeast expression systems and mammalian cell culture systems also can be used.

Example 13: Preparation of antibodies to cancer associated antigens

The recombinant cancer associated antigens produced as in Example 12 above are used to generate polyclonal antisera and monoclonal antibodies according to standard procedures. The antisera and antibodies so produced are tested for correct recognition of the cancer associated

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antigens by using the antisera/antibodies in assays of cell extracts of patients known to express the particular cancer associated antigen (e.g. an ELISA assay). These antibodies can be used for experimental purposes (e.g. localization of the cancer associated antigens, immunoprecipitations, Western blots, etc.) as well as diagnostic purposes (e.g., testing extracts of tissue biopsies, testing for the presence of cancer associated antigens).

Example 14: Expression of cancer associated antigens in cancers of similar and different origin.

The expression of one or more of the cancer associated antigens is tested in a range of tumor samples to determine which, if any, other malignancies should be diagnosed and/or treated by the methods described herein. Tumor cell lines and tumor samples are tested for cancer associated antigen expression, preferably by RT-PCR according to standard procedures. Northern blots also are used to test the expression of the cancer associated antigens. Antibody based assays, such as ELISA and western blot, also can be used to determine protein expression. A preferred method of testing expression of cancer associated antigens (in other cancers and in additional same type cancer patients) is allogeneic serotyping using a modified SEREX protocol (as described above for gastric clones).

In all of the foregoing, extracts from the tumors of patients who provided sera for the initial isolation of the cancer associated antigens are used as positive controls. The cells containing recombinant expression vectors described in the Examples above also can be used as positive controls.

The results generated from the foregoing experiments provide panels of multiple cancer associated nucleic acids and/or polypeptides for use in diagnostic (e.g. determining the existence of cancer, determining the prognosis of a patient undergoing therapy, etc.) and therapeutic methods (e.g., vaccine composition, etc.).

Example 15: HLA typing of patients positive for cancer associated antigen

To determine which HLA molecules present peptides derived from the cancer associated antigens, cells of the patients which express the cancer associated antigens are HLA typed.

30 Peripheral blood lymphocytes are taken from the patient and typed for HLA class I or class II, as

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well as for the particular subtype of class I or class II. Tumor biopsy samples also can be used for typing. HLA typing can be carried out by any of the standard methods in the art of clinical immunology, such as by recognition by specific monoclonal antibodies, or by HLA allele-specific PCR (e.g. as described in WO97/31126).

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Example 16: Characterization of breast cancer associated antigen peptides presented by MHC class I and class II molecules.

Antigens which provoke an antibody response in a subject may also provoke a cell-mediated immune response. Cells process proteins into peptides for presentation on MHC class I or class II molecules on the cell surface for immune surveillance. Peptides presented by certain MHC/HLA molecules generally conform to motifs. These motifs are known in some cases, and can be used to screen the breast cancer associated antigens for the presence of potential class I and/or class II peptides. Summaries of class I and class II motifs have been published (e.g., Rammensee et al., Immunogenetics 41:178-228, 1995). Based on the results of experiments such as those described in Example 15, the HLA types which present the individual breast cancer associated antigens are known. Motifs of peptides presented by these HLA molecules thus are preferentially searched.

One also can search for class I and class II motifs using computer algorithms. For example, computer programs for predicting potential CTL epitopes based on known class I motifs has been described (*see*, *e.g.*, Parker et al, *J. Immunol*. 152:163, 1994; D'Amaro et al., *Human Immunol*. 43:13-18, 1995; Drijfhout et al., *Human Immunol*. 43:1-12, 1995). HLA binding predictions can conveniently be made using an algorithm available via the Internet on the National Institutes of Health World Wide Web site at URL http://bimas.dcrt.nih.gov. Methods for determining HLA class II peptides and making substitutions thereto are also known (e.g. Strominger and Wucherpfennig (PCT/US96/03182)).

The lung cancer SEREX clone polypeptides NY-LU-12 and NY-LU-12B (variant B), SEQ ID NOs: 708 and 710, were subjected to the HLA binding peptide analysis described above, using the NIH website, to identify HLA binding peptides for several common HLA molecules (HLA-A1, A2, A3, A24, B7, B44, and B52). The results are listed below in Table 12.

Table 12: Identification of HLA binding peptides in lung SEREX clones

amino acids of

				animo acias or	
		<u>HLA</u>	<u>peptide</u>	NY-LU-12 protein	SEQ ID NO
		A1	NVEE-HSFSY	67 - 75	713
			PVDP-NILDY	287 - 295	714
	5		DTDY-RSMEY	398 - 406	715
		A 2	SLLE-DAIGC	506 - 514	716
			TLMI-QDKEV	521 - 529	717
			YVSSLDFWYC	533 - 542	718
	10		VIVEVLEPYV	671 - 680	719
			KLTD-WNKLA	948 - 956	720
			QLSDLHKQNL	975 - 984	721
			KQSEQELAYL	991 - 1000	722
			KLVDKEDIDT	1042 - 1051	723
	15		VMFA-RYKEL	1114 - 1122	724
;= mag					
ū		A 3	QMFG-YGQSK	417 - 425	725
			GMPVKNLQLK	481 - 490	726
'n			GLPE-EEEIK	823 - 831	727
IU.	20		LLCRRQFPNK	958 - 967	728
i W		A24	EYRD-VDHRL	405 - 413	729
18			GYVC-VEFSL	499 - 507	730
			DYGY-VCVEF	497 - 505	731
ij.	25		WYCKRCKANI	540 - 549	732
			TYPQPQKTSI	574 - 583	733
154			IYRSTPPEVI	663 - 672	734
13			HYYQ-GKKYF	754 - 762	735
10.22	20		VYVP-QDPGL	816 - 824	736
	30	В7	TOTO CONTRACTOR TO THE PARTY OF	26 25	727
		В/	WNRDYPPPPL MPPV-DPNIL	26 - 35	737 738
			TARD-AQRDL	285 - 293 432 - 440	739
			GPSEEKPSRL	448 - 457	73 <i>9</i> 740
	35		TPPEVIVEVL	667 - 676	741
	33		RVMFARYKEL	1113 - 1122	742
			WINI MUTULE	1113 1122	744
		B44	REMG-SCMEF	272 - 280	743
			EEQSSDAGLF	376 - 385	744
	40		KEYN-TGYDY	490 - 498	745
			TEAKQELITY	566 - 575	746
			VEALRVVKIL	710 - 719	747
			GEYG-GDSDY	906 - 914	748
			LERREREGKF	1000 - 1009	749

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		B52	RQDGESKTIM	650 - 659	750
			TPPEVIVEVL	667 - 676	751
			YGFIDLDSHV	701 - 710	752
			RQFP-NKEVL	962 - 970	753
	5				
		NY-L	U-12B (variant	. B)	
		A1	NVEE-HSFSY	121 - 129	754
	10		PVDP-NILDY	341 - 349	755
			DTDY-RSMEY	452 - 460	756
		A 2	WQSA-RFYYL	41 - 49	757
		n.	SLLE-DAIGC	560 - 568	
	15		TLMI-QDKEV	575 - 583	758
	15				759
			YVSSLDFWYC	587 - 596 735 - 734	760
l"i			VIVEVLEPYV	725 - 734	761
1111			KLTD-WNKLA	1002 - 1010	762
10 000	20		QLSDLHKQNL	1029 - 1038	763
1 ₃	20		KQSEQELAYL	1045 - 1054	764
: L			KLVDKEDIDT	1096 - 1105	765
field the part was bridge only dealer			VMFA-RYKEL	1168 - 1176	766
LII II		A 3	QMFG-YGQSK	471 - 479	767
12.00	25		GMPVKNLQLK	535 - 544	768
171			GLPE-EEEIK	877 - 885	769
			LLCRRQFPNK	1012 - 1021	770
121		A24	YYLN-ATDVL	47 - 55	771
122	30		FYYLNATDVL	46 - 55	772
			EYRD-VDHRL	459 - 467	773
			GYVC-VEFSL	553 - 561	774
			DYGY-VCVEF	551 - 559	775
			WYCKRCKANI	594 - 603	776
	35		TYPQPQKTSI	628 - 637	777
			IYRSTPPEVI	717 - 726	778
			HYYQ-GKKYF	808 - 816	779
			VYVP-QDPGL	870 - 878	780
	40	ם מו	LIMINIVINA	00 00	m 0 -
	40	B7	WNRDYPPPPL	80 - 89	781
			MPPV-DPNIL	339 - 347	782
			TARD-AQRDL	486 - 494	783
			GPSEEKPSRL	502 - 511	784
			TPPEVIVEVL	721 - 730	785
	45		RVMFARYKEL	1167 - 1176	786

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	B44	SEAWSSNEKF	59 - 68	787
		REMG-SCMEF	326 - 334	788
		EEQSSDAGLF	430 - 439	789
		KEYN-TGYDY	544 - 552	790
5		TEAKQELITY	620 - 629	791
		VEALRVVKIL	764 - 773	792
		GEYG-GDSDY	960 - 968	793
		LERREREGKF	1054 - 1063	794
10	B52	RQDGESKTIM	704 - 713	795
		TPPEVIVEVL	721 - 730	796
		YGFIDLDSHV	755 - 764	797
		RQFP-NKEVL	1016 - 1024	798

Likewise, other clones identified herein can be analyzed for the presence of candidate HLA binding peptides using no more than routine experimentation.

Example 17: Identification of the portion of a cancer associated polypeptide encoding an antigen

To determine if the cancer associated antigens isolated as described above can provoke a cytolytic T lymphocyte response, the following method is performed. CTL clones are generated by stimulating the peripheral blood lymphocytes (PBLs) of a patient with autologous normal cells transfected with one of the clones encoding a cancer associated antigen polypeptide or with irradiated PBLs loaded with synthetic peptides corresponding to the putative protein and matching the consensus for the appropriate HLA class I molecule (as described above) to localize an antigenic peptide within the cancer associated antigen clone (*see*, e.g., Knuth et al., *Proc. Natl. Acad. Sci. USA* 81:3511-3515, 1984; van der Bruggen et al., *Eur. J. Immunol.*24:3038-3043, 1994). These CTL clones are screened for specificity against COS cells transfected with the cancer associated antigen clone and autologous HLA alleles as described by Brichard et al. (*Eur. J. Immunol.* 26:224-230, 1996). CTL recognition of a cancer associated antigen is determined by measuring release of TNF from the cytolytic T lymphocyte or by ⁵¹Cr release assay (Herin et al., *Int. J. Cancer* 39:390-396, 1987). If a CTL clone specifically recognizes a transfected COS cell, then shorter fragments of the cancer associated antigen clone transfected in that COS cell are tested to identify the region of the gene that encodes the peptide. Fragments of the cancer associated antigen clone are prepared by

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exonuclease III digestion or other standard molecular biology methods. Synthetic peptides are prepared to confirm the exact sequence of the antigen.

Optionally, shorter fragments of cancer associated antigen cDNAs are generated by PCR. Shorter fragments are used to provoke TNF release or ⁵¹Cr release as above.

Synthetic peptides corresponding to portions of the shortest fragment of the cancer associated antigen clone which provokes TNF release are prepared. Progressively shorter peptides are synthesized to determine the optimal cancer associated antigen tumor rejection antigen peptides for a given HLA molecule.

A similar method is performed to determine if the cancer associated antigen contains one or more HLA class II peptides recognized by CTLs. One can search the sequence of the cancer associated antigen polypeptides for HLA class II motifs as described above. In contrast to class I peptides, class II peptides are presented by a limited number of cell types. Thus for these experiments, dendritic cells or B cell clones which express HLA class II molecules preferably are used.

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EQUIVALENTS

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

All references disclosed herein are incorporated by reference in their entirety.

We claim:

SEQ ID NO. 1:

5 U72994, AC004022, Z68323, AE001160, L34078, AF064863, AC002132, U60440, X66494, N21242, AA678312, W86762, R01605, AA782843, AA275156, W41927, AA874648, AA571241, AA562747, W10480, AA451301, AA866631, AA466667, AA999057, AI029140.

10 SEQ ID NO. 2:

AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648, AC004022, U72994, AC002420, AC004125, AA690961, W41927, AA874648.

SEQ ID NO. 3:

X98371, AL009008, L31790, Z83220, X92946, AC003975, AF008916, U80460, X75544, X66732, X95275, X52177, X07976, AC004451, Z74307, AB000878, AL009179, AF038667, Z78544, Z48008, U23486, J05096, AB000882, Z30213, L11593, U18530, L27325, AC005191, M99579, AA130270, AA158245, AA903098, AI018453, AA436455, AA980593, AA172479, AA637487, AA116588, AA426854, AA050404, AA390025, AI006618, AI048382, C85944, AA673480, AI006510, AA823338, AA413694, W35075, AA015033, AA413584, W29693, AA637069, AA619839, AA125149, AA039004, AA674696, AA871138, AA414747, AA198099, C91478, F071359, AA925957, AA820054, H16496, AI043756, AA892435, AA893551, AA818669, AA892785, AA944026, D33919, N96570, F19798, AI045451, AA800662, D65187, AA944025, AA925731, AA892314, AA945449.

30 SEQ ID NO. 4:

AA900930, AA925665.

35 SEQ ID NO. 5:

U58105, Z81485, Z54236, Z48584, U61375, M55267, M59856, X51942, U77302, Z48621, AF032455, Z11866, AB013392, L32792, AA871997, AA084083, AA130829, AA083063, AA666290, N38894, D54459, T28921, AA806015, AA512059, AI043087, AI042894, AA968324, AA238493, AA237462, AI042885, AI046424, AI035670, AA269430, AA250621, AI035540, AA260613, AA106870, AA238658, AA106134, AI042683, AA105958, AA144007, AA986558, AA457910, AA389400, AA673056, AA153254, AA754678, AI021109, AA390813, C36687, T41571, AI011183, AI013356, AI011739, AI030260, AA924384, C44421.

SEQ ID NO. 6:

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AF036717, U91327, AF036718, U56248, Z48795, Z99290, M30697, U58204, M24417, AF022983, M33581, AC004619, H64641, AA477478, AA369676, AA088359, AA057574,

AA683066, AA446279, AA332363, T09328, R80982, AA069486, AA410842, C18527, AA293033, H12730, AA287344, AA029631, R83063, AA061290, AA185993, AA880204. AA499308, AA183172, AA242360, AA792388, AA175587, AA277140, AA880395, AA899046, AA859550, C35363, C35702, C32682, F14140, T18049, C83149, T45787, AA924623, D47525, Z30723, AA897884, AA042465, AI009871, AA875198, C83016.

SEQ ID NO. 7:

X74116, AL022148, AC004548, AC000352, Z11664, Z78065, Z74028, AE000163, AE000750, X74229, D90700, R59414, AA176708, W02568, AA354664, R43017, AA973553, F10008, D61827, AA826300, Z41398, T77572, R40189, H85823, W86541, T17276, AA679337, X83357, AA184845, AA416260, AA475603, AA388692, AA764445, AA388689, AA219880, AA290020, AA388507, AA387267, C86741, AA414436, AA451259, AA413796, AA930916,

AA793690, AA619447, AA062257, AA522026, AA816247, AA892032, AA817702, H33461, AA925507, AA849449, AI029236, AA247069, AA697975, AA882508, AA893258, AA698410, AA891755, AA698227, AA892782, AA899328, T04373, AA567522, AA698408, AA202615, AA141016, AA697974, AA697998, C61176, D69691, AI030205, AA586054.

SEQ ID NO. 8:

U08218, L38909, Y11095, AC002431, Z23069, S77418, U39060, L38580, AF053367, Z36506, M18102, J03624, AA102264, AA730686, H47968, AA357170, AA130974, C06054,

- AA626429, F00559, AA604528, AA383348, AA040127, N84965, D54884, D54883, R94309, AA373184, AA128091, W68194, H58283, R76347, AA343938, AA305144, AI049611, AA384516, AA720553, N57395, R97387, D52674, AA169408, H66293, AA456362, T74258, AA730145, AA101952, N86388, AA355003, AA307640, AA385679, AA354542, N99075, N83528, H87678, R84494, R35720, AA670111, AA186452, W32370, D55392, W05161,
- AA641280, AA120503, C77063, AA146393, AA620177, AA509478, C77481, AA427148, AA474531, W83304, AA207424, AA763436, AA958473, AA799243, AA493061, AA967792, AA145256, AA089338, AA756259, AA789767, AA980112, AA866640, AA914516. AA821675, AA466770, AA015387, AA816036, AA246546, AA941789, AA955779, AA997768, AA997534, T43805, AA956150, T18836, T23333, AA525666, T18787, AA800483,

C64685, AA851367, C91730, AA143899, T23399. 35

SEQ ID NO. 9:

- AP000056, U43491, Z74919, L81498, Z94054, AC002503, L81499, AA740188, AA630241, AA974724, AA806907, N88859, N98242, H12649, R06485, R06511, AA546258, C76846, AA208416, AA959219, AA276381, W10055, AA462844, AA444278, W13447, W97802, AA542324, AA137880, AA269331, AA175695, W59029, AA003372, AA146233, AI045761, C93154, C94084, C94208, D68027, C12780, AA687005, AA080598, C12876, C12390,
- AA848674, AA924440, T15031, AA451569, H35524.

SEQ ID NO. 10:

U25640, AA127328, H24207, H08275, AA283063, AA826096, AA417382, AA464874, W05562, AA453370, N51211, AA495859, R33871, H00927, AA623997, AA220442, AA178568, AA605493, AA394557, AA956116, AA999037, AA818246.

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SEQ ID NO. 11:

AB001740, AF039956, AA581972, AA594539, AA236870, AA464410, AA237069, AA694199, AI038896, AA167314, AA577381, AA430117, N23143, R53610, W37647,

AA724229, AA313202, AA860618, W16866, AA134966, AA255556, AA305224, R50528, AA844913, W32042, W37383, AA908394, W93357, W31353, R55254, N79251, AA456077, AA477700, AA477701, AA989005, AA455580, N32722, N22935, R50622, AA135047, R51941, T34020, T30416, T32309, AA883332, W93445, AA166984, AA026749, T08224, AA255572, W03768, AA033670, W31880, AA772832, AA230974, AA511207, W82274,

15 AA230365, AA671085, AA511230, AA606681, AA023735, AA444535, W98518, W14718, W85455, AA980318, AA137525, AA035840, AA692158, AA007919, W48013, AA444534, AA981497, AA002566, W48089, W99869, AA960396, AA960580, AA145259, AA145683, AA388960, AA389941, AA266272, AA145124, AA267212, AA959753, AA407991, A175818, AA943997, AA899476, AA899756, AA943998, AA955446, AA012783, AA924956,

20 AA892219, AA955331, AI012225, AA891436.

SEQ ID NO. 12:

U72994, AC004022, AF043493, U43252, U43251, U81830, U58105, U68242, Z93242, AL009029, M29872, U12980, M81118, M30471, Z56258, AF012943, AC004080, AC002563, AF024533, AF002991, Z63771, AP000042, AF064863, U80017, AC004087, Z55235, L05920, AA508139, N90748, AA450240, AA948158, AA828938, AA165115, AI003312, AA436633, AA419100, AA743442, AA961990, AA885286, AA861312, T84801, AI040166, AA494115,

AA652324, AA181105, AA095541, R59256, AA503712, AA700364, AA603821, T60326, AA779097, AI023884, AA603785, H79111, W39526, AA506607, W94361, N66078, R01605, H22694, W86762, W99303, AA745640, AA678312, AA431870, W41927, AA874648, C92734, C23102, C53080, C91168, D65098, C32959, C50029, M80125, C34452, C83862, C24659, T21473, AA874720, C06696, W43071, AI043300, C53907.

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in the second

SEQ ID NO. 13:

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10 SEQ ID NO. 15:

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SEQ ID NO. 16:

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40 SEQ ID NO. 17:

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- 30 AA417423, AA470325, AA680491, AA754048, Z92686, T44319.

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SEQ ID NO. 19:

45 AE000500, AF030178, X66784, Z49405, M69106, M27174, X55037, AF004104, X78560, U51281, L17405, M10122, AC003106, X55122, X05553, AC002368, AF004101, U77066, U77456, X58072, AA481578, AA280143, AA481271, AA280144, AA736516, AA780050, AA359089, R82883, AA355987, AA571000, AA563168, AA738653, AA620225, AA855746, AA572293, AA530645, W40812, AA690944, AA839456, X61848, AA525648, AA944854,

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SEQ ID NO. 20:

5 Z99496, AC004518, AC004219, Z70204, J03925, Z66494, AC003053, U40072, AC002980, S52165, AB009051, M81884, AL021767, Z68164, M18044, J04145, AA383216, AA928132, Z19212, R84841, H83829, T71075, AA723804, H95329, AJ003438, W13441, AA199243, AA242009, AA272568, AA009230, AA880181, AA265864, AA124746, AA801108,

10 AA874804.

SEQ ID NO. 21:

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SEQ ID NO. 22:

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SEQ ID NO. 23:

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35 SEQ ID NO. 28:

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5 SEQ ID NO. 29:

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45 SEQ ID NO. 37:

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SEQ ID NO. 103:

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SEQ ID NO. 109:

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SEQ ID NO. 119:

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SEQ ID NO. 121:

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SEQ ID NO. 123:

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SEQ ID NO. 125:

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SEQ ID NO. 127:

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SEQ ID NO. 131:

AB002374, X51966, AL021367, AF036702, U88822, AF045642, U55815, AC004518, L13696, AL021889, U75395, AC002554, AC003103, X90386, X04981, U58334.

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SEQ ID NO. 133:

U48587, U68267, AF001906, AF033856, M33336, U73177, J03685, AC004743, AC004539, Z60442, N53159, N75331, AI042621, AA435593, AA608757, AA076290, AA662552, AA213762, AA630025, R57980, N24985, AA813323, H21646, H05642, AA359799, AA191039, AA318867, H15234, AA323419, N27160, AA636826, AA656934, AA726211, AA619507, AA792581, W59642, AA035921, AA637995, AA667370, AA592134, AA637894, AA591158, AA756070, AA467467, AA739462, AA272875, AA214985, AA739083, AA914526, AA386742, AA919409, AI046649, W35790, AA016357, W97992, AA656026, AA414710, AI006426, AA673795, AA239695, AA285593, AA615757, AA038932, AA073580, AA103792, AA220731, C85146, AA867112, AA028705, AA118743, AI005830, AA874206, AA451006, AA667719, AA637623, AA492608, AI048487, AA189854, AA116581, AA096759, R04321, R04399, Z48427, R04620, R04065, R04404, R04422, R03209, C51162, C44210, R05229, C49234, R03208, R04273, D75630, D75447, D75141, D74833, D74636, D74299, D70237, R05254, C42102, AA658642, AA685519, AA799735, C93660, AA685980,

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SEQ ID NO. 135:

AA750619.

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SEQ ID NO. 137:

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SEQ ID NO. 139:

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H29052, AA573543, T16608, AA773472, AA775416, AA601919, AA470534, AA351521,

AI015318, AA351163, AA486365, AA470985, AA565376, AA344993, R92629, AA553555, AA740903,

AA090392, H94289, AA457592, AI033503, T69709, R94066, AA040853, AA065296, AA349058, AA703759, T05287, H86075, AA043080, AA669995, AA737864, AA726753, AA727154, AA546638, AA222375, AA671227, AA032828, W14856, W33789, AA874531, AA982359, AA965843, AA965737, AA800560, AI035042, AA941796, AA390686, AA735566, AA802030, C74658, AA246925, AA803435, C27952, AA944566, AA817514, C83561, AA978443, C24959, C82705, C72516, H34014, AA712916, AA820781, D21893, D15866.

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SEQ ID NO. 141:

S45630, AF007162, X95383, AF029793, M55534, X60351, S77138, S77142, S74229, X60352, M63170, M24906, M28638, J03849, M12016, M73741, U04320, M12014, M24092, L08078, S53164, U26661, M12015, M25770, U16124, X87114, D29960, X14789, X85205, M17247, U05569, U66584, M26142, U47921, U47922, V01219, X95382, AP000007, AE000869, AB009529, AF062537, D10457, S37449, X59541, AA742442, AA704135, AA211774, N35834, AA482745, AA211607, N28898.

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SEQ ID NO. 143:

U78082, L78810, U14573, AC004068, U07561, M98511, AC004673, AA613346, AA953216, AA305926, H92800, R98218, AA629543, AA297666, AA302982, AA429481, AA126005, AA837225, AA856961, AA946848, F13749, AA847704, AA833896, AA621381, AA833875, AA459962, H22141, N73060, AA491955, H28477, AA224463, AA708753, AA152253, AI028510, AA483606, AA992126, T54783, AA715075, AA568204, AA715173, N64587, AA570740, AA984258, AA904211, H94979, AA085410, AA599352, AA488620, AA574442, AI049845, AA593471, AA393830, AA610509, AA297145, AA113272, AA835889, AA655005, AA689351, R93919, AA613761, AA550989, AA303054, H07953, AA713815, AA827490, AA865262, AA461308, H73550, AA657835, AA362349, H82679, AA378682, AA577755, AA663472, AA490602, AA857673, AA347114, AI049630, AA086150, AI017251, AA877992, AA084609, AI050760, AA808998, AA503258, AA613138, AA603156, AA513293, R97934, AA610233, AA654874, AA501867, AA604831, N22058, AA492114, T50676, AA757426, AA584482, AA789192, AI004591, T50694, AA862227, AA594145, AA728911, AA847499, AA159978, AA534204.

SEQ ID NO. 145:

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Z69030, L42375, U37352, D26445, U38192, U38191, U37770, U38190, U37353, U59418, L76702.

45 SEQ ID NO. 147:

L07872, L34544, L34543, X17459, S63463, M81871, L08904, U60093, U60094, L07873, L07874.

SEQ ID NO. 149:

U07158, X85784, AJ000541, U76832, L20821, AC003089, AC004504, AF049236, L40609, AF053765, L14677, Z94056, Z18277, AE001073, U85969, X79283, AJ223473, AA632339, AA732931, AA610556, AA973899, AA598896, AA531553, AA826535, AI000209, AA290836, AA642711, AA085920, W22275, D20744, UMGS017, AA487868, AA487869, AA085919, 682 AA833281, AA619252, C77541, AA691960, AA763615, AA164051, AA259589, AA060475, AA254185, AA666705, AA272597, AA152985, AI011416, AA850008, H33152, AA941811.

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SEQ ID NO. 151:

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15

SEQ ID NO. 153:

U28918, U17714, X82021, Z98048, D17265, D17092, Z82022, L04270.

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SEQ ID NO. 155:

X54859, Z86000, AC003043, X77738, X77737, L35930, AC003084, AC000111, M89651, AP000031, U67588, X03991, AC004660, AL010261, V01515, M86251, L29376, Z71417, L78442, U00921, AC004692, AC003698, AE000742, Z49128, Z73417, Z71418, AA424638, AA442084, AA805748, AA835489, AA713576, AA502343, AA765949, AA812332, AA831755, AA417718, AA776946, AA152295, AA731660, R48791, AA150237, N51650, N52616, N52586, AA533556, AA305755, AA760877, AA729913, AA731659, AA910594, AA904521, AA372550, R48898, N50390, R08712, H83343, AA417867, AA090407, AA009846, AA927286, AA678135, AI033148, AI041408, AA235113, AA398662, M62215, W27276, AA885767, AA460155, AA742433, R19908, AA040696, AA555240, AA043160, AA292844, R53160, AA536080, N70013, N35921, N70096, AA277029, AA560610, AI046716, AA237153, W15784, AA547132, AA231089, AA170968, D46090, C61892, C64408, D34777, D35175, D35914, D37381, AA559708, D37143, C60784, AI008855, AI021808, AI009216, D68214, AA220863, D70434.

SEQ ID NO. 157:

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U43195, U58512, U61266, D89493, U36909.

SEQ ID NO. 159:

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AF069442, AF001295, M13820, M10081, AB010077, AA491075, AA446881, AA588390, AA479958, N20112, R86178, R97894, T64868, W68074, AA365195, AA928749, AI037069, AA882303, AA791693, AA822133, AI037224, AA404165, AI036575, AA499662, AA864136, AA561223, AA183703, AA647218, AA792208, W48100, D40621, AJ225487, AA294595,

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SEQ ID NO. 161:

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SEQ ID NO. 163:

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X15183, AF028832, D87666, J04633, L33676, X07270, U94395, M27024, M30627, X16857, X07265, M36830, M30626, AA669137, AA725103, AA890496, AA314095, AA554815, AA313331, AA730100, AA214035, AA876412, AA121630, AA314010, AA927532, AA968674, AA679253, N66271, AA558907, AA309988, AA587079, AA075436, AA160964, AA205657, AA214083, AA130903, AA917032, AA149623, AA857523, AA889843, AA305037, AA491055, W73240, AA255644, W73295, AA765431, AA178947, N66409, AA074895, AA306976, AA075052, AA075387, AA130892, AA857443, AA405942, AA629891, AA152004, AA129550, W56527, AA513807, AA703828, AA223171, C75280, AA889155, AA854676, AA773063, AA774999, AA152392, AA307057, AA316954, AA657352, AA522607, AA188113, AA026444, AI003623, AA312717, AA312400, T64299, AA178992, AA228992, AI042136, AA457613, AI032857, AA164461, AA625127, AA807763, AA130815, AA054695, AA937097, W93534, N67875, AA526896, W52802, AA527942, N34251, W28646, AA668543, AA496091, W52511, AA070581, AA306826, AA120908, AA699607, AA086423, N72134, AA630369, AA564649, AA046806, AA666249, AA306893, AA225404, AA127417, AA854951.

SEQ ID NO. 165:

- M23885, AF047868, AF017732, AB005249, Z83229, AF026483, U97194, Z67884, Z67881, X13481, X07651, AC001226, AC002542, AB002307, AA984684, AA017533, AA306600, AA261957, F08123, R17885, AA282208, H85861, H85836, AA593150, H87276, AA057384, AA243602, AA013399, AA374926, AA721341, R88896, AA021538, AA101740, AA375314, AA090398, H86058, AA984556, AA215816, AA092672, AA034243, AA328017, F11174,
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SEQ ID NO. 167:

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Y11251, AF030234, AF043945, L40407.

AA239037, AA672620, AA915168, AA863498, AA123378.

SEQ ID NO. 169:

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U33822, X61838, AA572230, AA589570, AA929790, AA104830, C81582, AA271190, AA290278, AA543616, AI043207, AA107832, AA958460, AI020992, AA795905, AA277468, AA475069, AA111610, AA389139, AA154163.

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SEQ ID NO. 170:

D32050, D16969, AC004423, S81497.

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SEQ ID NO. 172:

D86982, L07131, M14544, AA296228, AA318436, AA296234, H88394, W26642, AF038251, AA394101, N35855, N56791, N35444, AA147382, AA647547, AA939939, AA895989, AA122437, AA277698, W75741, AI036117, AA980469, AA033178, AI006694, AA980625, AA033190, AA175922, AA172918, AA895209, AA028700, AA416048, AA175247, AA217057, AI045760, R64866, D40836, D41873, AA509279, D40089, AA114361, AA751642,

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SEQ ID NO. 174:

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40 SEQ ID NO: 176

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L37107, AF060514, S77819, X13058, D86070, U50395, U07182, U90328, Y08900, M75144, Y08901, U74487, U48619, K01700, M13872, AF051368, U48616, U48618, X00741, M13874, M13873, X01237, U48617, M22887, X54156, U94788, M13115, U41451, U41452, X01236, K02110, U59757, M22895, M13118, U63714, M22888, M13116, M22894, M13117, U51857, U37120, U62133, U07020, X91793, L07907, U26741, U59758, S78456, L23634, U22145,

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SEQ ID NO: 177

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SEQ ID NO: 178

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AA894190, C20441, AA231739, D68624, AA964536, AT000114, D22968.

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AA398766, R48359, AA426107, AA909990, AI017459, AA076224, N39533, AI026941, AA412699, AA292828, AI024759, AI016910, AA573306, R48386, AA065307, AA774549, AI016070, AA884918, AA431512, AA306051, AA476440, AA292924, AA621059, AA411830, AA405079, AA596171, AA989987, AA472637, AA690249, AA691927, AA792720,

- 5 AA637983, AA020137, AA097337, AA117759, W17615, AA285526, AA111347, AA208823, AA879750, AA413058, W33316, AA161891, W41259, AA511152, AA027481, AA020252, AA033106, AA965045, D41048, AI031042, D48020, AA925258, D40853, AA945674, C19585, AI013412, T15040, AA541011, AA990782, AA851306, AA540938, T23386, AA783863, AA979035, AA951002, AA438957, AA979006, AA978995, AA800046, AA556128, C27411,
- 10 D15562, T20348, AA966363, AA949269, AA785774, AA728671, D16092, N37869, D48782.

SEQ ID NO: 179

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SEQ ID NO: 180

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SEQ ID NO: 181

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D86999, AL008633, AB010395, Z37999, AC002295, AC002397, AC003033, AL021878, X97651, AC003957, M33387, AP000053, AL009048, AC003046, M88481, Z74044, L81611, X75284, AA261777, AA864889, AI028372, AA465521, AA846126, AA262767, AA204697, AA215375, H51473, AA506924, AA502898, AA377435, AA113921, D62650, H22351, H51430, H22382, AA465101, C18637, W39589, AA327239, R40889, AA873226, AA460243, AA621037, H59359, AA725078, T74486, AA862185, H67186, AA830023, AA443869, AA828666, N38846, AA345908, AA525207, AA609559, AA628297, AA663165, T94643, R05610, R71812, D80739, AA677926, W04238, AA136929, AA137096, AA565152, N46909, N70293, W74325, H63794, N29751, N27675, AI036841, AA840246, AA833063, AA615467. AA499981, W87950, AA968257, C81326, AA575315, AA198626, AA177237, W83702, 10 AA032570, AA143960, W76885, C81402, AA624565, C81370, AA790518, AA462820, AA198544, AA619130, AA763304, AA408798, AA596445, AA388381, AA208825, AA465777, AA123453, AA163963, AA272421, AA387128, AA119389, AA004024, AA048596, AA178783, AA408740, AA462137, AA763879, AA104287, AA536743, AA189208, AA474607, AA119325, AA930111, AA591279, AA110900, AA511170, Z36370, 15 AA915493, AA799054, C76955, AA475573, AA409880, AA608394, W40814, AA177344. AA139563, AA185921, AA103715, AA087674, W84211, AA413195, AA472014, AA718145, C76233, AA797276, W10301, AA982386, AA607099, AA123778, AA189429, W76777, AA408982, AA274777, C79658, AA543812, AA290119, R75266, AA060786, AA544015. 20 AA537758, AA237310, R02919, AA858989, AA695540, AA848230, H74756, AA979969, AA924645, AA964247, AA952521, AA997784, T36746, AI012428, AI045470, AI045012, AA963263, T02640, AA514153, AA685633, H35763, AA246073, AA875723, T38957, AA685944, T36529, AA951284, C93715, AA735681, T36773, AA926109, AA899894, D22301, T36428, T38528, AA550561, AA824716, AA818438, AA951260, AA698348.

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15 SEQ ID NO: 270

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30 SEQ ID NO: 278

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30 SEQ ID NO: 280

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35 SEQ ID NO: 316

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- 45 AA294340, AA898159, C61838, D69030, AA850706, D65552, C62086, AA851036, C52237, AA925983, C32833, AA294788, AI030007, AA998684, AI011286, AA800269, AI009727,

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- AA096992, W81949, W75269, AA789988, AA259316, AA790623, AI021000, W57110, AA990198, AA067249, AA726260, AA537135, AA798563, AA755019, AA030169,

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5 SEQ ID NO: 321

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45 SEQ ID NO: 328

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- 45 SEQ ID NO.420

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35 SEQ ID NO: 471

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15 SEQ ID NO: 473

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25 SEQ ID NO: 479

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10 SEQ ID NO: 490

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25 SEQ ID NO: 491

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40 SEQ ID NO: 499

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20 SEQ ID NO: 507

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- 40 AA076343, AA296715, AA076342, AA353626, AA015595, AA081221, R83719, AA334546, H51631, AA343126, T85486, W22495, AA129429, T20065, R96799, AA443644, T78812, AA864764, N53004, W48656, AA599769.

45 SEQ ID NO: 514

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5 SEQ ID NO: 519

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20 SEQ ID NO: 532

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15 SEQ ID NO: 537

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40 SEQ ID NO: 539

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40 SEQ ID NO:597

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- 45 AA675673, AA522332, AA863643, AA816116, AA553002, AA210060, AA396324,

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5 SEQ ID NO:666

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- 45 AA697379.

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D15134, RICC0136A Rice cDNA, partial sequence (C0136A).	4.3
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D46618, RICS11395A Rice cDNA, partial sequence (S11395_1A). 36	5 4.3
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D46719, RICS11572A Rice cDNA, partial sequence (S11572_1A). 36	5 4.3
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AA802334, AA802334 GM04219.5prime GM Drosophila melanogaster	. 36 4.3
D46066, RICS10470A Rice cDNA, partial sequence (S10470_1A). 36	5 4.3
D47037, RICS12104A Rice cDNA, partial sequence (S12104_1A). 36	5 4.3
	5 4.3
D47174, RICS12340A Rice cDNA, partial sequence (S12340_2A). 36	5 4.3
T04578, T04578 625 Lambda-PRL2 Arabidopsis thaliana cDNA clon	36 4.3
C83675, C83675 Oryctolagus cuniculus corneal endothelial cDN 36 4	3
	5 4.3
R90044, R90044 16399 Lambda-PRL2 Arabidopsis thaliana cDNA cl	36 4.3
D46994, RICS12013A Rice cDNA, partial sequence (S12013_2A). 36	5 4.3
AA440820, AA440820 LD15713.5prime LD Drosophila melanogaster	36 4.3
C72089, C72089 Rice cDNA, partial sequence (E0963_1A) 36 4.	3
Z84004, SSZ84004 S.scrofa mRNA; expressed sequence tag (5'; 36 4	.3
D47519, RICS13070A Rice cDNA, partial sequence (S13070_1A). 36	5 4.3
C19735, C19735 Rice cDNA, partial sequence (E10858_1A) 36 4	.3
D47231, RICS12462A Rice cDNA, partial sequence (S12462_1A). 36	5 4.3
D47147, RICS12293A Rice cDNA, partial sequence (S12293_1A). 36	5 4.3
AA950198, AA950198 LD30147.5prime LD Drosophila melanogaster	36 4.3
Z47624, ATTS4480 A. thaliana transcribed sequence; clone TAI 36 4	.3
	5 4.3
D47137, RICS12280A Rice cDNA, partial sequence (S12280_1A). 36	5 4.3
· · · · · · · · · · · · · · · · · · ·	4.3
AA392275, AA392275 LD11117.5prime LD Drosophila melanogaster	36 4.3

SEQ ID NO:546

D87455, D87455 Human mRNA for KIAA0266 gene, complete cds Z99129, HS425C14 Human DNA sequence from clone 425C14 on chr... 42 0.20 D90900, D90900 Synechocystis sp. PCC6803 complete genome, 2/... 40 0.80 Z74281, SCYDL233W S.cerevisiae chromosome IV reading frame O... 38 3.1 AL021528, HS394P21 Homo sapiens DNA sequence from PAC 394P21... 38 3.1 Z49155, HSL83D3 Human DNA from cosmid L83d3, Huntington's Di... 38 3.1 U33761, HSU33761 Human cyclin A/CDK2-associated p45 (Skp2) mR... 38 3.1 AF052832, AF052832 Trypanosoma cruzi CL Brener cosmid 1b21 ch... 38 3.1 Z98600, SPAC20G4 S.pombe chromosome I cosmid c20G4 38 3.1

Y09438, SPHUSPLUS S.pombe hus1+ gene 38 3.1 D29951, MUSKIF Mouse mRNA for kinesin family protein KIF1a, ... 38 3.1

HUMAN ESTs

AA151187, AA151187 zo03c11.r1 Stratagene colon (#937204) Homo... 694 0.0
AA824593, AA824593 oc83d10.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 670 0.0
AA954862, AA954862 op20c03.s1 NCI_CGAP_Co12 Homo sapiens cDNA... 581 e-164
T16360, T16360 NIB1193 Normalized infant brain, Bento Soares ... 517 e-145
R54592, R54592 yg81h10.s1 Homo sapiens cDNA clone 40102 3'. 511 e-143
AA373594, AA373594 EST85631 HSC172 cells I Homo sapiens cDNA ... 507 e-142
AA100660, AA100660 zl90a05.r1 Stratagene colon (#937204) Homo... 383 e-104
R42009, R42009 yg05b04.s1 Homo sapiens cDNA clone 31336 3'. 379 e-103
AA249614, AA249614 k3041.seq.F Human fetal heart, Lambda ZAP ... 252 5e-65
AA360633, AA360633 EST69800 T-cell lymphoma Homo sapiens cDNA... 182 4e-44
AA053498, AA053498 zl70b11.r1 Stratagene colon (#937204) Homo... 38 1.5
AA992442, AA992442 or85h03.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 38 1.5

AA065677, AA065677 mm43c03.rl Stratagene mouse melanoma (#937... 297 4e-79 AA529728, AA529728 vi38g12.rl Beddington mouse embryonic regi... 42 0.035 W91608, W91608 MTA.D10.092.A MTA adult mouse thymus library M... 42 0.035 AA177186, AA177186 mt51a11.rl Stratagene mouse embryonic carc... 42 0.035 AA048008, AA048008 mj26h10.rl Soares mouse embryo NbME13.5 14... 36 2.2 AA637535, AA637535 vu10c02.rl Barstead mouse myotubes MPLRB5 ... 36 2.2 AA726355, AA726355 vu90c09.rl Stratagene mouse skin (#937313)... 36 2.2 AA404025, AA404025 va31c11.rl GuayWoodford Beier mouse kidney... 36 2.2 AA606014, AA060014 ml34d07.rl Stratagene mouse testis (#93730... 36 2.2 AA870617, AA870617 vq23h10.rl Barstead stromal cell line MPLR... 36 2.2 AA414112, AA414112 vc64f08.sl Knowles Solter mouse 2 cell Mus... 36 2.2 AA764250, AA764250 vv49e09.rl Soares 2NbMT Mus musculus cDNA ... 36 2.2

H34350, H34350 EST111226 Rat PC-12 cells, NGF-treated (9 days... 36 1.9 C40718, C40718 C.elegans cDNA clone yk247f9 : 5' end, single... 36 1.9 AA817925, AA817925 UI-R-A0-af-g-04-0-UI.s1 UI-R-A0 Rattus nor... 36 1.9 AA955650, AA955650 UI-R-E1-fc-e-10-0-UI.s1 UI-R-E1 Rattus nor... 36 1.9

SEQ ID NO:547

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.35
U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.35
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.35
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4
AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4

HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI CGAP Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 3e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121174, AA121174 zl88g08.sl Stratagene colon (#937204) Homo... 317 2e-84 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.17 AA888147, AA888147 04h11.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 40 0.67 AA946650, AA946650 oq38h09.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA806381, AA806381 oc22g05.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 40 0.67 AA577174, AA577174 nm86e11.s1 NCI CGAP Co9 Homo sapiens cDNA ... AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... AA262229, AA262229 zs25b12.s1 NCI CGAP GCB1 Homo sapiens cDNA... 40 0.67 AA969632, AA969632 op38h05.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. AI005324, AI005324 ou13h07.x1 Soares NFL_T_GBC S1 Homo sapien... AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA814296, AA814296 nz07d08.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 40 0.67 AA873216, AA873216 oh70f04.s1 NCI_CGAP Kid5 Homo sapiens cDNA... 40 0.67 AA403143, AA403143 zv66d01.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.67 W45005, W45005 zc05c12.rl Soares parathyroid tumor NbHPA Homo... 40 0.67 W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.67 AA974988, AA974988 on59b06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 Homo sapien... AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. 40 0.67 R02514, R02514 ye70b08.r1 Homo sapiens cDNA clone 123063 5'. 40 0.67 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.67 AA877455, AA877455 ob33g01.s1 NCI CGAP Kid5 Homo sapiens cDNA... AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.67

2761

AA903406, AA903406 ok62c11.s1 NCI CGAP GC4 Homo sapiens cDNA ... 40 0.67 AA461270, AA461270 zx63b07.r1 Soares total fetus Nb2HF8 9w Ho... 40 0.67 AA927863, AA927863 om18a08.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 AA587486, AA587486 nn84e09.s1 NCI_CGAP_Br2 Homo sapiens cDNA ... 40 0.67 W47466, W47466 zc34h02.rl Soares senescent fibroblasts NbHSF ... 40 0.67 AA022495, AA022495 ze70e04.s1 Soares fetal heart NbHH19W Homo... 40 0.67 AA460961, AA460961 zx63b07.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.67 AA393904, AA393904 zt85e06.rl Soares testis NHT Homo sapiens ... 40 0.67 AA872272, AA872272 oh72a11.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.67 W47341, W47341 zc34h02.s1 Soares senescent fibroblasts NbHSF ... N72024, N72024 yz96g01.s1 Homo sapiens cDNA clone 290928 3'. 40 0.67 N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'. 40 0.67 AA813115, AA813115 aj44d06.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA826741, AA826741 85f12.s1 NCI_CGAP Pr24 Homo sapiens cDNA... 40 0.67 AA160827, AA160827 zo62e01.s1 Stratagene pancreas (#937208) H... 40 0.67 AI040354, AI040354 oy33d12.x1 Soares_parathyroid tumor NbHPA ... 40 0.67 AA573297, AA573297 nk98d09.s1 NCI_CGAP Co3 Homo sapiens cDNA ... 40 0.67 AA416559, AA416559 zu18c03.rl Soares NhHMPu S1 Homo sapiens c... 40 0.67 AA401079, AA401079 zv66d01.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.67 AI005204, AI005204 ou60c12.x1 NCI CGAP Br2 Homo sapiens cDNA ... 40 0.67 N21678, N21678 yx63g01.s1 Soares melanocyte 2NbHM Homo sapien... 40 0.67 AA824270, AA824270 aj29f01.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA804907, AA804907 oa89a01.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 40 0.67 AA759038, AA759038 ah75h11.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA417295, AA417295 zu18c03.s1 Soares NhHMPu S1 Homo sapiens c... AA628544, AA628544 af27h12.s1 Soares total fetus Nb2HF8 9w Ho... AA618498, AA618498 np30a11.s1 NCI CGAP Pr22 Homo sapiens cDNA... 40 0.67 AA503727, AA503727 ne49g02.s1 NCI CGAP Co3 Homo sapiens cDNA ... 40 0.67 AA514777, AA514777 ni24b01.sl NCI CGAP Co4 Homo sapiens cDNA ... 40 0.67 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.67 AA770473, AA770473 ah89h06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.67 AA759377, AA759377 ah54a10.s1 Soares testis NHT Homo sapiens ... 40 0.67 AA629243, AA629243 zu77e03.s1 Soares testis NHT Homo sapiens ... AA262162, AA262162 zs25b12.rl NCI CGAP GCB1 Homo sapiens cDNA... 40 0.67 AA161105, AA161105 zo58c05.s1 Stratagene pancreas (#937208) H... AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.6 AA948291, AA948291 oq34d02.s1 NCI CGAP GC4 Homo sapiens cDNA ... AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.6 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.6 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.6 H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'. 38 2.6 R82551, R82551 yi19d06.r1 Homo sapiens cDNA clone 149195 5'. 38 2.6

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5... 40 0.24 AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14... 40 0.24 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.24 AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 40 0.24 AI048515, AI048515 uh61e08.rl Soares mouse embryonic stem cel... 40 0.24 AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM... 40 0.24 AA009071, AA009071 mg87b11.rl Soares mouse embryo NbME13.5 14... 40 0.24 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.24 AA497479, AA497479 vh29b12.r1 Soares mouse mammary gland NbMM... 40 0.24 AA038869, AA038869 mi95b10.r1 Soares mouse p3NMF19.5 Mus musc... 40 0.24 AA790448, AA790448 vw04f09.rl Soares mouse mammary gland NbMM... 40 0.24 AA881111, AA881111 vz06e09.r1 Soares mouse mammary gland NbMM... 40 0.24 AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14... 40 0.24 W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus... AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.24 AA000268, AA000268 mg32e09.rl Soares mouse embryo NbME13.5 14... 40 0.24 AI047077, AI047077 uh61g06.r1 Soares mouse embryonic stem cel... 40 0.24 AA543280, AA543280 vi80h05.r1 Soares mouse mammary gland NbMM... 40 0.24 AA106301, AA106301 ml81a09.rl Stratagene mouse kidney (#93731... 40 0.24 AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 40 0.24 AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM... W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.24 AA049011, AA049011 mj48c09.r1 Soares mouse embryo NbME13.5 14... 40 0.24 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... AA138067, AA138067 mq37c11.r1 Barstead MPLRB1 Mus musculus cD... 40 0.24 AA475425, AA475425 vh20g09.r1 Soares mouse mammary gland NbMM... 40 0.24 AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.24 AA016868, AA016868 mh36e12.r1 Soares mouse placenta 4NbMP13.5... AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.24 AA833479, AA833479 uc91c03.rl Soares mouse uterus NMPu Mus mu... W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.24 AA033481, AA033481 mi42b07.rl Soares mouse embryo NbME13.5 14... AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.94 AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM... 36 3.7 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 3.7 AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu... 36 3.7 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 3.7 AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 3.7 W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M... AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 3.7 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... AA591243, AA591243 vm18c04.rl Knowles Solter mouse blastocyst... 36 3.7

AI047609, AI047609 uh63g07.rl Soares mouse embryonic stem cel... 36 3.7

AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.7

AA966976, AA966976 ua38f11.rl Soares mouse mammary gland NbMM... 36 3.7

AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... 36 3.7

W20935, W20935 mb96c07.rl Soares mouse p3NMF19.5 Mus musculus... 36 3.7

AA230661, AA230661 mw15f08.rl Soares mouse 3NME12 5 Mus musculus ... 36 3.7

AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 3.7

AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu... 36 3.7

AA089210, AA089210 mo05d10.rl Stratagene mouse lung 937302 Mu... 36 3.7

AA08925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... 36 3.7

AA793845, AA793845 vr35e12.rl Barstead mouse macrophage (#9... 36 3.7

AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... 36 3.7

AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 ... 36 3.7

AA645119, AA645119 vs72d03.rl Stratagene mouse skin (#937313)... 36 3.7

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.053 C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84 AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... 38 0.84 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84 C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.84 AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.84 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... 38 0.84 AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.84 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... 38 0.84 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.84 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... 38 0.84 AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... 38 0.84 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.84 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.3 AA125602, AA125602 JM00M011.QM3 Miracidia Sic 3/96 Schistosom... 36 3.3 D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). 36 3.3 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... C68472, C68472 C.elegans cDNA clone yk305a12:5' end, singl... 36 3.3 AA785775, AA785775 h4b05a1.f1 Aspergillus nidulans 24hr asexu... D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A). AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.3 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.3 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.3 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.3

SEQ ID NO:548

U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.34
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.34
U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.34
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.3
AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.3
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.3
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.3

HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI_CGAP_Co2 Homo sapiens cDNA ... 363 3e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.16 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.64 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.64 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... AA573297, AA573297 nk98d09.s1 NCI_CGAP_Co3 Homo sapiens cDNA ... N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. AA888147, AA888147 04h11.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 40 0.64 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... AA877455, AA877455 ob33g01.s1 NCI_CGAP Kid5 Homo sapiens cDNA... R02514, R02514 ye70b08.rl Homo sapiens cDNA clone 123063 5'. 40 0.64 AA514777, AA514777 ni24b01.s1 NCI_CGAP_Co4 Homo sapiens cDNA ... 40 0.64 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.5 N98472, N98472 yy65a04.r1 Homo sapiens cDNA clone 278382 5'. 38 2.5 AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.5 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.5 AA948291, AA948291 oq34d02.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.5

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA469884, AA469884 vf71g10.rl Barstead mouse pooled organs MP... 40 0.23 AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.23 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.23 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.23 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.23 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.23 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.23 AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.91 AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 ... 36 3.6 AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... W20935, W20935 mb96c07.rl Soares mouse p3NMF19.5 Mus musculus... 36 3.6 AA966976, AA966976 ua38f11.rl Soares mouse mammary gland NbMM... AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu... 36 3.6 AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.6 W87202, W87202 mf55g08.rl Soares mouse embryo NbME13.5 14.5 M... 36 3.6 AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu... 36 3.6 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 3.6 AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c... 36 3.6 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... AA645119, AA645119 vs72d03.rl Stratagene mouse skin (#937313)... 36 3.6 AA230661, AA230661 mw15f08.rl Soares mouse 3NME12 5 Mus muscu... 36 3.6 AA824205, AA824205 vy20g08.rl Stratagene mouse macrophage (#9... 36 3.6 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36, 3.6 AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 3.6 AA591243, AA591243 vm18c04.r1 Knowles Solter mouse blastocyst... 36 3.6 AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... AA530735, AA530735 vj32g11.rl Stratagene mouse diaphragm (#93... 36 3.6 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... 36 3.6 W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M... AA089210, AA089210 mo05d10.rl Stratagene mouse lung 937302 Mu... 36 3.6 AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM... AA542324, AA542324 vk53e07.rl Stratagene mouse Tcell 937311 M... 36 3.6

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.052 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.81 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.81 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.81 D46069, RICS10475A Rice cDNA, partial sequence (S10475_1A). 36 3.2 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.2 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.2 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.2 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 3.2 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 3.2

D45997, RICS10346A Rice cDNA, partial sequence (S10346_1A). 36 3.2 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.2 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 3.2 C68472, C68472 C.elegans cDNA clone yk305a12 : 5' end, singl... 36 3.2 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.2 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.2 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.2

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SEQ ID NO:549

U79271, HSU79271 Human clones 23920 and 23921 mRNA sequence 650 0.0
AC000395, AC000395 Genomic sequence from Human 9q34, complete 42 0.28
AC004636, AC004636 Homo sapiens chromosome 5, P1 clone 1268h6 42 0.28
M94579, HUMCEL Human carboxyl ester lipase (CEL) gene, comple 42 0.28
AC002097, AC002097 Homo sapiens chromosome 9q34, clone 246H5, 42 0.28
AB006709, AB006709 Vibrio alginolyticus rpoN gene for RNA po 42 0.28
Z47074, CEK07C10 Caenorhabditis elegans cosmid K07C10, compl 40 1.1
AC004755, AC004755 Homo sapiens chromosome 19, fosmid 37502, 40 1.1
Z28051, SCYKL051W S.cerevisiae chromosome XI reading frame O 40 1.1
AF022655, AF022655 Homo sapiens cep250 centrosome associated 40 1.1
AB006708, AB006708 Arabidopsis thaliana genomic DNA, chromos 40 1.1
AF049105, AF049105 Homo sapiens centrosomal Nek2-associated p 40 1.1
Z28050, SCYKL050C S.cerevisiae chromosome XI reading frame O 40 1.1
X75781, SCXI286K S.cerevisiae chromosome XI (28.6 kb) DNA fo 40 1.1
Y16899, DMY16899 Drosophila melanogaster mRNA for optomotor 38 4.3
M87854, RATBARK1 Rattus norvegicus beta-adrenergic receptor k 38 4.3
M74822, RATMHTLL Rat MHC class I TL-like protein gene, comple 38 4.3
M80776, HUMBARK1A Human beta-adrenergic receptor kinase 1 mRN 38 4.3
D84549, YSACA Candida tropicalis DNA for carnitine acetyltra 38 4.3
L23127, RATRMCI Rattus norvegicus germline MHC class I gene, 38 4.3
AC004257, AC004257 Homo sapiens chromosome 19, cosmid R33209, 38 4.3
U70850, CELF28F9 Caenorhabditis elegans cosmid F28F9 38 4.3
U88309, CELT23B3 Caenorhabditis elegans cosmid T23B3 38 4.3
X53421, DVCHOS18 D. virilis s18, s15, s19, s16 chorion prote 38 4.3
D89245, D89245 Schizosaccharomyces pombe mRNA, partial cds, 38 4.3
AF009623, AF009623 Parascaris univalens PUMA1 (puma1) mRNA, c 38 4.3
S48813, S48813 beta-adrenergic receptor kinase [rats, brain, 38 4.3
Z67883, CEK02A4 Caenorhabditis elegans cosmid K02A4, complet 38 4.3
U90567, GGU90567 Gallus gallus glutamine rich protein mRNA, p 38 4.3
M98498, BOVEZRINA Bos taurus ezrin mRNA, complete cds. 38 4.3
M34073, MUSMHT10C Mus musculus (clone T10-c) MHC class I cell 38 4.3

S81843, S81843 beta-adrenergic receptor kinase 1 [Syrian hams... 38 4.3 X61157, HSBARK H.sapiens mRNA for beta-adrenergic receptor k... 38 4.3 U08438, HSNBARKS4 Human beta-adrenergic receptor kinase (ADRB... 38 4.3 U39674, CELC06E2 Caenorhabditis elegans cosmid C06E2. 38 4.3

HUMAN ESTs

W29097, W29097 56d11 Human retina cDNA randomly primed sublib... 1045 0.0 AA886109, AA886109 ny44f05.s1 NCI CGAP Pr12 Homo sapiens cDNA... 656 0.0 AA829894, AA829894 oe51e12.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 650 0.0 AA879456, AA879456 oj91g03.s1 Soares NFL T GBC S1 Homo sapien... 650 0.0 AA029201, AA029201 zk12f08.sl Soares pregnant uterus NbHPU Ho... 650 0.0 AA102109, AA102109 zk87g11.s1 Soares pregnant uterus NbHPU Ho... 650 0.0 AA843811, AA843811 ak09c08.s1 Soares parathyroid tumor NbHPA ... 650 0.0 W72147, W72147 zd70f08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0 N51485, N51485 yz04e06.s1 Homo sapiens cDNA clone 282082 3'. 650 0.0 AI033069, AI033069 ow93f02.s1 Soares fetal liver spleen 1NFLS... 642 0.0 AA161465, AA161465 zo73a06.s1 Stratagene pancreas (#937208) H... 638 0.0 N51277, N51277 yz14d07.s1 Homo sapiens cDNA clone 283021 3'. 636 e-180 N64528, N64528 yz91e06.s1 Homo sapiens cDNA clone 290434 3'. 636 e-180 H99906, H99906 yx32h10.s1 Homo sapiens cDNA clone 263491 3'. 636 e-180 AA812519, AA812519 ai79b03.s1 Soares testis NHT Homo sapiens ... 636 e-180 R71679, R71679 vi85e08.s1 Homo sapiens cDNA clone 155558 3'. 628 e-178 AA744290, AA744290 ny51d02.s1 NCI CGAP Pr18 Homo sapiens cDNA... 626 e-177 AI038590, AI038590 ox34e03.s1 Soares total fetus Nb2HF8 9w Ho... 624 e-177 AA099913, AA099913 zk87g11.rl Soares pregnant uterus NbHPU Ho... 624 e-177 AA083859, AA083859 zn16d06.s1 Stratagene neuroepithelium NT2R... 622 e-176 AA883684, AA883684 al58a05.s1 Soares NFL T GBC S1 Homo sapien... 613 e-173 R39448, R39448 yc95d03.s1 Homo sapiens cDNA clone 23921 3'. 593 e-167 R36854, R36854 vf52c07.s1 Homo sapiens cDNA clone 25899 3'. 591 e-167 H98684, H98684 yx17g01.s1 Homo sapiens cDNA clone 262032 3'. 585 e-165 R07471, R07471 ye97a06.s1 Homo sapiens cDNA clone 125650 3'. 581 e-164 AA910762, AA910762 ol25h06.s1 Soares NFL T GBC S1 Homo sapien... 559 e-157 AA083954, AA083954 zn17d06.s1 Stratagene neuroepithelium NT2R... 555 e-156 AA346369, AA346369 EST52776 Fetal heart II Homo sapiens cDNA ... 545 e-153 R54092, R54092 yg98d07.s1 Homo sapiens cDNA clone 41818 3'. 539 e-151 H09074, H09074 y197a06.s1 Homo sapiens cDNA clone 46164 3'. 535 e-150 N21975, N21975 yw30c10.s1 Homo sapiens cDNA clone 253746 3'. 533 e-149 D59844, HUM070E11A Human fetal brain cDNA 3'-end GEN-070E11. 466 e-129 H11525, H11525 ym15h07.s1 Homo sapiens cDNA clone 48232 3'. 442 e-122 AA971254, AA971254 op73c08.s1 Soares NFL T GBC S1 Homo sapien... 442 e-122 W77907, W77907 zd70f08.rl Soares fetal heart NbHH19W Homo sap... 428 e-118 AA878973, AA878973 oj26d11.s1 NCI_CGAP_Kid3 Homo sapiens cDNA... 389 e-106 AA715235, AA715235 nv10g01.s1 NCI CGAP Pr22 Homo sapiens cDNA... 357 2e-96

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AA328928, AA328928 EST32475 Embryo, 12 week I Homo sapiens cD... 355 7e-96 AA860455, AA860455 aj80f02.s1 Soares parathyroid tumor NbHPA ... 283 2e-74 AA026096, AA026096 ze97a04.rl Soares fetal heart NbHH19W Homo... 268 1e-69 AA026516, AA026516 ze97a04.s1 Soares fetal heart NbHH19W Homo... 172 6e-41 T26899, T26899 ESTDIR509 Homo sapiens cDNA clone CDDIR509 3'. N71178, N71178 yw30c10.rl Homo sapiens cDNA clone 253746 5'. 165 le-38 AA372290, AA372290 EST84170 Raji cells, cyclohexamide treated... 98 3e-18 AI038890, AI038890 ox84g12.x1 Soares senescent fibroblasts Nb... 40 0.53 D81647, HUM180D08B Human fetal brain cDNA 5'-end GEN-180D08. 38 2.1 AA452630, AA452630 zx33f08.rl Soares total fetus Nb2HF8 9w Ho... 38 2.1 AA682624, AA682624 zi19g01.s1 Soares fetal liver spleen 1NFLS... 38 2.1 AA742364, AA742364 ny89c12.s1 NCI CGAP GCB1 Homo sapiens cDNA... 38 2.1 AA907234, AA907234 ol03h08.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 38 2.1 T09391, T09391 EST07284 Homo sapiens cDNA clone HIBBT71 5' en... 38 2.1 AA161236, AA161236 zo59h07.s1 Stratagene pancreas (#937208) H... 38 2.1 AA252941, AA252941 zr50g09.rl Soares NhHMPu S1 Homo sapiens c... 38 2.1 AA252245, AA252245 zr64g07.s1 Soares NhHMPu S1 Homo sapiens c... 38 2.1 AA780678, AA780678 ac70h01.s1 Stratagene fetal retina 937202 ... 38 2.1 W05501, W05501 za84a12.rl Soares fetal lung NbHL19W Homo sapi... 38 2.1 AI039908, AI039908 ox25f07.x1 Soares_total_fetus_Nb2HF8_9w Ho... 38 2.1 AA280664, AA280664 zs99f09.s1 NCI CGAP GCB1 Homo sapiens cDNA... 38 2.1 AA973566, AA973566 oo46f09.s1 NCI_CGAP Lu5 Homo sapiens cDNA ... 38 2.1 N27253, N27253 yx17g01.rl Homo sapiens cDNA clone 262032 5'. AA995707, AA995707 os29c09.s1 NCI_CGAP Kid5 Homo sapiens cDNA... 38 2.1 AI016407, AI016407 ot72e09.s1 Soares total fetus Nb2HF8 9w Ho... N70619, N70619 za84a12.s1 Homo sapiens cDNA clone 299230 3'. AA242923, AA242923 zr64g07.r1 Soares NhHMPu S1 Homo sapiens c... 38 2.1 AA938631, AA938631 0096f07.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... 38 2.1 AA985290, AA985290 am74g03.s1 Stratagene schizo brain S11 Hom... 38 2.1

AA690806, AA690806 vt25h10.r1 Barstead mouse myotubes MPLRB5 ... 377 e-103 AA155014, AA155014 mr99h05.r1 Stratagene mouse embryonic carc... 180 8e-44 AA269966, AA269966 va57d06.r1 Soares mouse 3NME12 5 Mus muscu... 172 2e-41 AA089195, AA089195 mo05h11.r1 Stratagene mouse lung 937302 Mu... 163 2e-38 AA466212, AA466212 vg86g02.r1 Barstead mouse pooled organs MP... 68 8e-10 AA423476, AA423476 ve76d07.r1 Soares mouse mammary gland NbMM... 60 2e-07 AA597213, AA597213 vo28a05.r1 Barstead mouse irradiated colon... 40 0.19 AA396266, AA396266 vb45c01.r1 Soares mouse lymph node NbMLN M... 40 0.19 AA967806, AA967806 uh05d06.r1 Soares mouse hypothalamus NMHy ... 38 0.75 AA591111, AA591111 vm12c06.r1 Knowles Solter mouse blastocyst... 38 0.75 AA153891, AA153891 mq56e05.r1 Soares 2NbMT Mus musculus cDNA ... 38 0.75

AI019772, AI019772 ua90h02.rl Soares mouse mammary gland NbMM... AA472253, AA472253 vh10g05.rl Soares mouse mammary gland NbMM... 36 3.0 AA230895, AA230895 mw14g07.r1 Soares mouse 3NME12 5 Mus muscu... 36 3.0 W18052, W18052 mb83g03.rl Soares mouse p3NMF19.5 Mus musculus... 36 3.0 AA797681, AA797681 vx66c12.rl Stratagene mouse skin (#937313)... 36 3.0 W66734, W66734 me26g05.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.0 AA968020, AA968020 uh07g01.r1 Soares mouse hypothalamus NMHy ... AA051644, AA051644 mj55d12.rl Soares mouse embryo NbME13.5 14... 36 3.0 AA162797, AA162797 mr29g09.rl Soares mouse 3NbMS Mus musculus... 36 3.0 AA549644, AA549644 vk80f08.s1 Knowles Solter mouse 2 cell Mus... 36 3.0 AA273295, AA273295 vc01e01.rl Soares mouse lymph node NbMLN M... 36 3.0 AA048480, AA048480 mj33d08.rl Soares mouse embryo NbME13.5 14... 36 3.0 AA098207, AA098207 mn83d01.rl Stratagene mouse Tcell 937311 M... 36 3.0 AA027381, AA027381 mi05c06.rl Soares mouse placenta 4NbMP13.5... 36 3.0 AA544474, AA544474 vk33h06.rl Soares mouse mammary gland NbMM... 36 3.0 AA416466, AA416466 vd15c09.s1 Knowles Solter mouse 2 cell Mus... 36 3.0 AA285999, AA285999 vb88h08.rl Soares mouse 3NbMS Mus musculus... AA175025, AA175025 ms85f06.rl Soares mouse 3NbMS Mus musculus... AA544386, AA544386 vk33f06.rl Soares mouse mammary gland NbMM... 36 3.0 AA175557, AA175557 ms96g04.rl Soares mouse 3NbMS Mus musculus... 36 3.0 AA711924, AA711924 vu59f09.rl Soares mouse mammary gland NbMM... 36 3.0 AA734052, AA734052 vv22c10.r1 Stratagene mouse heart (#937316... 36 3.0 W53738, W53738 md12a12.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.0 AA611837, AA611837 vo82a06.rl Barstead mouse myotubes MPLRB5 ... 36 3.0 AA879531, AA879531 vv96f06.rl Soares mouse mammary gland NbMM... 36 3.0 AA288625, AA288625 vb23g09.rl Soares mouse 3NbMS Mus musculus...

AA784124, AA784124 d2b06a1.f1 Aspergillus nidulans 24hr asexu... 38 0.67 AI044911, AI044911 UI-R-C1-kk-e-05-0-UI.s1 UI-R-C1 Rattus nor... 36 2.6 AA550452, AA550452 1605m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 2.6 F20017, ATTS6056 A. thaliana transcribed sequence; clone TAP... 36 2.6 AA786697, AA786697 k5d01a1.f1 Aspergillus nidulans 24hr asexu... 36 2.6 AA433457, AA433457 SW3ICA2345SK Brugia malayi infective larva... 36 2.6

SEQ ID NO:550

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.20 AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.20 U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.20 Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 0.80

AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA.... 40 0.80 Y14330, HSY14330 Homo sapiens partial mRNA for jagged2 protein 38 3.2 AF003521, AF003521 Homo sapiens Jagged 2 mRNA, complete cds 38 3.2 AF029778, AF029778 Homo sapiens Jagged2 (JAG2) mRNA, complete... 38 3.2 AF020201, AF020201 Homo sapiens Jagged 2 mRNA, complete cds 38 3.2 Z71523, SCYNL247W S.cerevisiae chromosome XIV reading frame ... 38 3.2 AF029779, AF029779 Homo sapiens hJAG2.del-E6 (JAG2) mRNA, alt... U70049, RNU70049 Rattus norvegicus jagged2 precursor gene, pa... 38 3.2 X96722, SCCHXIVL S.cerevisiae DNA region from chromosome XIV... 38 3.2 AF005938, AF005938 Cavia porcellus L-type voltage-dependent c... 38 3.2 X78972, SBSTRBF S.bluensis ISP 5564 genes strB and strF 38 3.2 X94912, HSPR22 H.sapiens Pr22 gene 38 3.2

HUMAN ESTs

AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0 AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-144 AA551799, AA551799 nk04a11.s1 NCI_CGAP_Co2 Homo sapiens cDNA ... 363 2e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 2e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 1e-90 AA121174, AA121174 zl88g08.sl Stratagene colon (#937204) Homo... 317 le-84 AA121198, AA121198 zl88g08.r1 Stratagene colon (#937204) Homo... 317 1e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.098 AI005204, AI005204 ou60c12.x1 NCI_CGAP_Br2 Homo sapiens cDNA ... 40 0.39 AA757360, AA757360 ah98a01.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AI005324, AI005324 ou13h07.x1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA416559, AA416559 zu18c03.rl Soares NhHMPu S1 Homo sapiens c... AA262162, AA262162 zs25b12.rl NCI CGAP GCB1 Homo sapiens cDNA... AA824270, AA824270 aj29f01.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA826741, AA826741 85f12.s1 NCI CGAP Pr24 Homo sapiens cDNA... AA813115, AA813115 aj44d06.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA403143, AA403143 zv66d01.rl Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA725024, AA725024 ah97h10.s1 Soares NFL T GBC S1 Homo sapien... AA804907, AA804907 oa89a01.s1 NCI CGAP GCB1 Homo sapiens cDNA... AA628544, AA628544 af27h12.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA618498, AA618498 np30a11.s1 NCI CGAP Pr22 Homo sapiens cDNA... 40 0.39 AA503727, AA503727 ne49g02.s1 NCI CGAP Co3 Homo sapiens cDNA ... 40 0.39 AA460961, AA460961 zx63b07.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA770473, AA770473 ah89h06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA759377, AA759377 ah54a10.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA629243, AA629243 zu77e03.s1 Soares testis NHT Homo sapiens ... AA903406, AA903406 ok62c11.s1 NCI CGAP GC4 Homo sapiens cDNA ... 40 0.39 AA215903, AA215903 hp0042.seq.F Fetal heart, Lambda ZAP Expre... 40 0.39

AA160827, AA160827 zo62e01.s1 Stratagene pancreas (#937208) H... 40 0.39 AA577174, AA577174 nm86e11.s1 NCI CGAP Co9 Homo sapiens cDNA ... 40 0.39 AA969632, AA969632 op38h05.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 N72025, N72025 yz96g02.s1 Homo sapiens cDNA clone 290930 3'. AA974988, AA974988 on59b06.sl Soares NFL T GBC Sl Homo sapien... W32428, W32428 zc05c12.s1 Soares parathyroid tumor NbHPA Homo... 40 0.39 N21678, N21678 yx63g01.s1 Soares melanocyte 2NbHM Homo sapien... 40 0.39 AA860208, AA860208 ak48c10.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA814296, AA814296 nz07d08.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 40 0.39 AA806381, AA806381 oc22g05.s1 NCI CGAP GCB1 Homo sapiens cDNA... 40 0.39 AA435587, AA435587 zt85d07.s1 Soares testis NHT Homo sapiens ... 40 0.39 W45005, W45005 zc05c12.rl Soares parathyroid tumor NbHPA Homo... 40 0.39 AA393904, AA393904 zt85e06.rl Soares testis NHT Homo sapiens ... 40 0.39 AA759038, AA759038 ah75h11.s1 Soares testis NHT Homo sapiens ... 40 0.39 AA927863, AA927863 om18a08.s1 Soares NFL T GBC S1 Homo sapien... 40 0.39 AA461270, AA461270 zx63b07.rl Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA417295, AA417295 zu18c03.s1 Soares NhHMPu S1 Homo sapiens c... 40 0.39 W47466, W47466 zc34h02.rl Soares senescent fibroblasts NbHSF ... 40 0.39 AA262229, AA262229 zs25b12.s1 NCI CGAP GCB1 Homo sapiens cDNA... 40 0.39 AA587486, AA587486 nn84e09.s1 NCI CGAP Br2 Homo sapiens cDNA ... 40 0.39 AA401079, AA401079 zv66d01.s1 Soares total fetus Nb2HF8 9w Ho... 40 0.39 AA872272, AA872272 oh72a11.s1 NCI CGAP Kid5 Homo sapiens cDNA... W47341, W47341 zc34h02.s1 Soares senescent fibroblasts NbHSF ... 40 0.39 N72024, N72024 yz96g01.s1 Homo sapiens cDNA clone 290928 3'. 40 0.39 N35076, N35076 yy19b08.s1 Homo sapiens cDNA clone 271671 3'. 40 0.39 AI040354, AI040354 oy33d12.x1 Soares parathyroid tumor NbHPA ... 40 0.39 AA946650, AA946650 oq38h09.s1 NCI CGAP Kid5 Homo sapiens cDNA... AA022495, AA022495 ze70e04.s1 Soares fetal heart NbHH19W Homo... 40 0.39 AA873216, AA873216 oh70f04.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.39 R82551, R82551 yi19d06.r1 Homo sapiens cDNA clone 149195 5'. 38 1.5 H30248, H30248 yp42a01.s1 Homo sapiens cDNA clone 190056 3'. 38 1.5 AA161105, AA161105 zo58c05.s1 Stratagene pancreas (#937208) H... 38 1.5 AA948291, AA948291 oq34d02.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... 38 1.5 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 1.5 AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 1.5 AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ...

AA616807, AA616807 vn68c05.r1 Barstead mouse irradiated colon... 180 6e-44
AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 40 0.14
AA543280, AA543280 vj80h05.r1 Soares mouse mammary gland NbMM... 40 0.14
AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14... 40 0.14
AA106439, AA106439 ml59a08.r1 Stratagene mouse testis (#93730... 40 0.14

AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14... 40 0.14 AA881111, AA881111 vz06e09.rl Soares mouse mammary gland NbMM... 40 0.14 AA049011, AA049011 mj48c09.r1 Soares mouse embryo NbME13.5 14... 40 0.14 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... 40 0.14 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.14 AA016868, AA016868 mh36e12.rl Soares mouse placenta 4NbMP13.5... 40 0.14 AA833479, AA833479 uc91c03.rl Soares mouse uterus NMPu Mus mu... 40 0.14 AA790448, AA790448 vw04f09.rl Soares mouse mammary gland NbMM... 40 0.14 AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM... AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.14 AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.14 AA497479, AA497479 vh29b12.rl Soares mouse mammary gland NbMM... 40 0.14 AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD... 40 0.14 AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 40 0.14 AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 40 0.14 AI048515, AI048515 uh61e08.rl Soares mouse embryonic stem cel... 40 0.14 W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.14 AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA000268, AA000268 mg32e09.rl Soares mouse embryo NbME13.5 14... 40 0.14 AA475425, AA475425 vh20g09.rl Soares mouse mammary gland NbMM... AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5... 40 0.14 AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM... 40 0.14 AA106301, AA106301 ml81a09.r1 Stratagene mouse kidney (#93731... 40 0.14 AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14... 40 0.14 W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.14 W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus... 40 0.14 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.14 AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.55 AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 2.2 AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... 36 2.2 AA239210, AA239210 mx89e02.r1 Soares mouse NML Mus musculus c... 36 2.2 AA824205, AA824205 vy20g08.rl Stratagene mouse macrophage (#9... 36 2.2 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 2.2 AA089210, AA089210 mo05d10.r1 Stratagene mouse lung 937302 Mu... 36 2.2 AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 ... 36 2.2 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... 36 2.2 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 2.2 AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 2.2 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... 36 2.2 AA218431, AA218431 my07e05.r1 Barstead mouse lung MPLRB2 Mus ... 36 2.2 AA796056, AA796056 vo65d01.r1 Soares mouse mammary gland NbMM... 36 2.2 AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 2.2 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 2.2 AI047609, AI047609 uh63g07.rl Soares mouse embryonic stem cel... 36 2.2 AA591243, AA591243 vm18c04.rl Knowles Solter mouse blastocyst... 36 2.2

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AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... 36 2.2 AA966976, AA966976 ua38f11.rl Soares mouse mammary gland NbMM... 36 2.2

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.031 AA801145, AA801145 EST190642 Normalized rat ovary, Bento Soar... 38 0.48 AI012760, AI012760 EST207211 Normalized rat placenta, Bento S... 38 0.48 AA874930, AA874930 UI-R-E0-ci-b-05-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48 C82607, C82607 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48 AA859865, AA859865 UI-R-E0-cc-b-04-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48 C83463, C83463 Oryctolagus cuniculus corneal endothelial cDN... 38 0.48 AA801144, AA801144 EST190641 Normalized rat ovary, Bento Soar... 38 0.48 AA859448, AA859448 UI-R-A0-bf-b-01-0-UI.s1 UI-R-A0 Rattus nor... AI009631, AI009631 EST204082 Normalized rat lung, Bento Soare... 38 0.48 AI009035, AI009035 EST203486 Normalized rat embryo, Bento Soa... 38 0.48 AA859542, AA859542 UI-R-E0-br-d-03-0-UI.s1 UI-R-E0 Rattus nor... 38 0.48 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... 36 1.9 AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 1.9 Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 1.9 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... 36 1.9 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 1.9 AA125602, AA125602 JM00M011.QM3 Miracidia Sic 3/96 Schistosom... 36 1.9 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... 36 1.9

SEQ ID NO:551

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.36
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.36
U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.36
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.4
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.4
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.4
AC004301, AC004301 Drosophila melanogaster DNA sequence (P1 D... 40 1.4

HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

276V

AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.s1 NCI CGAP Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121174, AA121174 zl88g08.s1 Stratagene colon (#937204) Homo... 317 2e-84 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.17 AA877455, AA877455 ob33g01.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.68 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.68 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.68 AA573297, AA573297 nk98d09.s1 NCI CGAP Co3 Homo sapiens cDNA ... 40 0.68 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.68 AA514777, AA514777 ni24b01.s1 NCI CGAP Co4 Homo sapiens cDNA ... 40 0.68 R02514, R02514 ye70b08.r1 Homo sapiens cDNA clone 123063 5'. 40 0.68 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.68 AA888147, AA888147 04h11.s1 NCI CGAP Co10 Homo sapiens cDNA... 40 0.68 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.68 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.7 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. 38 2.7 AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.7 AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.7 AA948291, AA948291 oq34d02.s1 NCI CGAP GC4 Homo sapiens cDNA ... 38 2.7 R14449, R14449 yf81h09.r1 Homo sapiens cDNA clone 29034 5'. AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.7

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA469884, AA469884 vf71g10.rl Barstead mouse pooled organs MP... 40 0.24 AA038869, AA038869 mi95b10.rl Soares mouse p3NMF19.5 Mus musc... 40 0.24 AA185487, AA185487 mt62c07.r1 Soares 2NbMT Mus musculus cDNA ... AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.24 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.24 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.24 AA250010, AA250010 mz59b12.rl Soares mouse lymph node NbMLN M... AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 0.97 AA139459, AA139459 mq86a03.r1 Stratagene mouse melanoma (#937... 38 0.97 AA881111, AA881111 vz06e09.rl Soares mouse mammary gland NbMM... AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 3.8 AA049011, AA049011 mj48c09.rl Soares mouse embryo NbME13.5 14... AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 36 3.8 AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 36 3.8

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AA840087, AA840087 uc99h12.rl Soares mouse uterus NMPu Mus mu 36 3.8
AA543280, AA543280 vj80h05.rl Soares mouse mammary gland NbMM 36 3.8
AA007762, AA007762 mg76b03.rl Soares mouse embryo NbME13.5 14 36 3.8
AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5 36 3.8
AA591243, AA591243 vm18c04.rl Knowles Solter mouse blastocyst 36 3.8
AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu 36 3.8
W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus 36 3.8
AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 36 3.8
AA856298, AA856298 vw99b01.r1 Soares 2NbMT Mus musculus cDNA 36 3.8
AA833479, AA833479 uc91c03.rl Soares mouse uterus NMPu Mus mu 36 3.8
AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus 36 3.8
AA089210, AA089210 mo05d10.rl Stratagene mouse lung 937302 Mu 36 3.8
AI047609, AI047609 uh63g07.r1 Soares mouse embryonic stem cel 36 3.8
AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM 36 3.8
AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD 36 3.8
W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus 36 3.8
AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M 36 3.8
AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313) 36 3.8
AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM 36 3.8
AA497479, AA497479 vh29b12.r1 Soares mouse mammary gland NbMM 36 3.8
W87202, W87202 mf55g08.rl Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA016868, AA016868 mh36e12.rl Soares mouse placenta 4NbMP13.5 36 3.8
AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus 36 3.8
AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14 36 3.8
AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM 36 3.8
AA530735, AA530735 vj32g11.rl Stratagene mouse diaphragm (#93 36 3.8
AA009071, AA009071 mg87b11.r1 Soares mouse embryo NbME13.5 14 36 3.8
AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 36 3.8
AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313) 36 3.8
AA106301, AA106301 ml81a09.r1 Stratagene mouse kidney (#93731 36 3.8
AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA 36 3.8
C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque 36 3.8
AA796056, AA796056 vo65d01.r1 Soares mouse mammary gland NbMM 36 3.8
AA230661, AA230661 mw15f08.rl Soares mouse 3NME12 5 Mus muscu 36 3.8
AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14 36 3.8
AA000268, AA000268 mg32e09.r1 Soares mouse embryo NbME13.5 14 36 3.8
AI048515, AI048515 uh61e08.r1 Soares mouse embryonic stem cel 36 3.8
W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA790448, AA790448 vw04f09.r1 Soares mouse mammary gland NbMM 36 3.8
AA824205, AA824205 vy20g08.r1 Stratagene mouse macrophage (#9 36 3.8
AA475425, AA475425 vh20g09.r1 Soares mouse mammary gland NbMM 36 3.8
W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
W77724, W77724 me84h06.r1 Soares mouse embryo NbME13.5 14.5 M 36 3.8
AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c 36 3.8
12 1237210, 120237210 Historouz.ii boates Hiouse Hittle Hitts Hiuseulus C 30 3.8

12

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AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... 42 0.055 AA891284, AA891284 EST195087 Normalized rat heart, Bento Soar... 40 0.22 Z83055, RNZ83055 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22 AI010967, AI010967 EST205418 Normalized rat muscle, Bento Soa... 40 0.22 AA852049, AA852049 EST194818 Normalized rat spleen, Bento Soa... 40 0.22 H33489, H33489 EST109542 Rat PC-12 cells, NGF-treated (9 days... 40 0.22 AA799616, AA799616 EST189113 Normalized rat heart, Bento Soar... 40 0.22 Z83044, RNZ83044 R.norvegicus mRNA; expressed sequence tag; ... 40 0.22 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.86 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.86 T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.86 AA785775, AA785775 h4b05a1.f1 Aspergillus nidulans 24hr asexu... 36 3.4 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... 36 3.4 C68472, C68472 C.elegans cDNA clone yk305a12: 5' end, singl... 36 3.4 AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... 36 3.4 Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... 36 3.4 AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.4 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp... Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.4 D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). 36 3.4 AA125602, AA125602 JM00M011.QM3 Miracidia Sjc 3/96 Schistosom... 36 3.4 AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.4 D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A).

SEQ ID NO:552

U66201, MMU66201 Mus musculus fibroblast growth factor homolo... 42 0.38
AF020738, AF020738 Mus musculus fibroblast growth factor-rela... 42 0.38
U66197, HSU66197 Human fibroblast growth factor homologous fa... 42 0.38
Z46966, MMIMOGN44 M.musculus mRNA for imogen 44. 40 1.5
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA,... 40 1.5
U85773, HSU85773 Human phosphomannomutase (PMM2) mRNA, comple... 40 1.5

HUMAN ESTs

W22160, W22160 63A6 Human retina cDNA Tsp509I-cleaved sublibr... 791 0.0 AA860926, AA860926 ak22d06.s1 Soares testis NHT Homo sapiens ... 650 0.0

276Y

AA348243, AA348243 EST54707 Hippocampus I Homo sapiens cDNA 5... 513 e-143 AA551799, AA551799 nk04a11.sl NCI CGAP Co2 Homo sapiens cDNA ... 363 4e-98 AA327309, AA327309 EST30621 Colon I Homo sapiens cDNA 5' end 353 4e-95 AA344913, AA344913 EST50856 Gall bladder II Homo sapiens cDNA... 337 2e-90 AA121198, AA121198 zl88g08.rl Stratagene colon (#937204) Homo... 317 2e-84 AA121174, AA121174 zl88g08.sl Stratagene colon (#937204) Homo... 317 2e-84 AA001561, AA001561 ze46e07.s1 Soares retina N2b4HR Homo sapie... 42 0.18 AA172158, AA172158 zp29a01.s1 Stratagene neuroepithelium (#93... 40 0.72 N35888, N35888 yy28b05.s1 Homo sapiens cDNA clone 272529 3'. 40 0.72 AA877455, AA877455 ob33g01.s1 NCI CGAP Kid5 Homo sapiens cDNA... 40 0.72 AA573297, AA573297 nk98d09.s1 NCI CGAP Co3 Homo sapiens cDNA ... 40 0.72 AA040802, AA040802 zf07g05.s1 Soares fetal heart NbHH19W Homo... 40 0.72 R02514, R02514 ye70b08.r1 Homo sapiens cDNA clone 123063 5'. 40 0.72 AA514777, AA514777 ni24b01.s1 NCI_CGAP_Co4 Homo sapiens cDNA ... 40 0.72 AA041240, AA041240 zf07g05.rl Soares fetal heart NbHH19W Homo... 40 0.72 AA888147, AA888147 04h11.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 40 0.72 AA039536, AA039536 zk39h10.s1 Soares pregnant uterus NbHPU Ho... 40 0.72 AA416734, AA416734 zu08c01.s1 Soares testis NHT Homo sapiens ... 38 2.8 N25839, N25839 yx22e05.rl Homo sapiens cDNA clone 262496 5'. AA431486, AA431486 zw72g01.s1 Soares testis NHT Homo sapiens ... 38 2.8 N98472, N98472 yy65a04.rl Homo sapiens cDNA clone 278382 5'. AA416815, AA416815 zu08c01.rl Soares testis NHT Homo sapiens ... 38 2.8 AA852281, AA852281 NHTBCae11g05r1 Normal Human Trabecular Bon... 38 2.8 AA948291, AA948291 oq34d02.s1 NCI CGAP GC4 Homo sapiens cDNA ... 38 2.8

AA616807, AA616807 vn68c05.rl Barstead mouse irradiated colon... 180 1e-43 AA185487, AA185487 mt62c07.rl Soares 2NbMT Mus musculus cDNA ... 40 0.26 AA276740, AA276740 vc42a12.r1 Soares mouse 3NbMS Mus musculus... 40 0.26 AA469884, AA469884 vf71g10.r1 Barstead mouse pooled organs MP... 40 0.26 AA230758, AA230758 my32g10.rl Barstead mouse pooled organs MP... 40 0.26 AA038869, AA038869 mi95b10.r1 Soares mouse p3NMF19.5 Mus musc... 40 0.26 AA106439, AA106439 ml59a08.rl Stratagene mouse testis (#93730... 40 0.26 AA763419, AA763419 vw54a12.rl Soares mouse mammary gland NMLM... 40 0.26 AA139459, AA139459 mq86a03.r1 Stratagene mouse melanoma (#937... 38 1.0 AA068686, AA068686 mm59a03.rl Stratagene mouse embryonic carc... 38 1.0 AA218431, AA218431 my07e05.rl Barstead mouse lung MPLRB2 Mus ... 36 4.0 AI047077, AI047077 uh61g06.rl Soares mouse embryonic stem cel... 36 4.0 C87249, C87249 Mus musculus fertilized egg cDNA 3'-end seque... 36 4.0 AI035925, AI035925 ub49e05.rl Soares mouse mammary gland NbMM... AA111190, AA111190 mp66b11.rl Soares 2NbMT Mus musculus cDNA ... 36 4.0 AA645119, AA645119 vs72d03.r1 Stratagene mouse skin (#937313)... 36 4.0 AA530735, AA530735 vj32g11.r1 Stratagene mouse diaphragm (#93... 36 4.0

AA000268, AA000268 mg32e09.r1 Soares mouse embryo NbME13.5 14... 36 4.0 AA793845, AA793845 vr35e12.rl Barstead mouse myotubes MPLRB5 ... AA840087, AA840087 uc99h12.r1 Soares mouse uterus NMPu Mus mu... AA711873, AA711873 vu28e06.rl Barstead mouse myotubes MPLRB5 ... AA790448, AA790448 vw04f09.rl Soares mouse mammary gland NbMM... 36 4.0 AA106301, AA106301 ml81a09.r1 Stratagene mouse kidney (#93731... 36 4.0 AA543280, AA543280 vi80h05.rl Soares mouse mammary gland NbMM... AA007762, AA007762 mg76b03.r1 Soares mouse embryo NbME13.5 14... AA921560, AA921560 vy52c06.rl Stratagene mouse lung 937302 Mu... 36 4.0 AA692425, AA692425 vt59b05.rl Barstead mouse irradiated colon... 36 4.0 AA833479, AA833479 uc91c03.rl Soares mouse uterus NMPu Mus mu... AA824205, AA824205 vy20g08.rl Stratagene mouse macrophage (#9... AA033481, AA033481 mi42b07.r1 Soares mouse embryo NbME13.5 14... 36 4.0 W61547, W61547 md57a02.r1 Soares mouse embryo NbME13.5 14.5 M... AA796056, AA796056 vo65d01.rl Soares mouse mammary gland NbMM... 36 4.0 AA467482, AA467482 ve01a10.r1 Soares mouse NbMH Mus musculus ... 36 4.0 AA239210, AA239210 mx89e02.rl Soares mouse NML Mus musculus c... AA881111, AA881111 vz06e09.rl Soares mouse mammary gland NbMM... AA542324, AA542324 vk53e07.r1 Stratagene mouse Tcell 937311 M... 36 4.0 AA089210, AA089210 mo05d10.rl Stratagene mouse lung 937302 Mu... W77724, W77724 me84h06.rl Soares mouse embryo NbME13.5 14.5 M... AI048515, AI048515 uh61e08.r1 Soares mouse embryonic stem cel... 36 4.0 AA009071, AA009071 mg87b11.rl Soares mouse embryo NbME13.5 14... AA475425, AA475425 vh20g09.r1 Soares mouse mammary gland NbMM... 36 4.0 AA230661, AA230661 mw15f08.r1 Soares mouse 3NME12 5 Mus muscu... AA138067, AA138067 mq37c11.rl Barstead MPLRB1 Mus musculus cD... W83172, W83172 mf09a06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 4.0 AA797372, AA797372 vw27b08.rl Soares mouse mammary gland NbMM... 36 4.0 AA711859, AA711859 vu59c10.rl Soares mouse mammary gland NbMM... AA967316, AA967316 vj47a03.r1 Stratagene mouse skin (#937313)... 36 4.0 W87202, W87202 mf55g08.r1 Soares mouse embryo NbME13.5 14.5 M... AA103139, AA103139 mo17f05.rl Life Tech mouse embryo 13 5dpc ... 36 4.0 AA014223, AA014223 mh20a03.rl Soares mouse placenta 4NbMP13.5... W62989, W62989 md88h12.r1 Soares mouse embryo NbME13.5 14.5 M... W20935, W20935 mb96c07.r1 Soares mouse p3NMF19.5 Mus musculus... AA966976, AA966976 ua38f11.r1 Soares mouse mammary gland NbMM... AA856298, AA856298 vw99b01.rl Soares 2NbMT Mus musculus cDNA ... AA014768, AA014768 mi66h04.r1 Soares mouse embryo NbME13.5 14... 36 4.0 AA497479, AA497479 vh29b12.rl Soares mouse mammary gland NbMM... AA049011, AA049011 mj48c09.r1 Soares mouse embryo NbME13.5 14... 36 4.0 AA016868, AA016868 mh36e12.rl Soares mouse placenta 4NbMP13.5... AI047609, AI047609 uh63g07.r1 Soares mouse embryonic stem cel... 36 4.0 AA591243, AA591243 vm18c04.rl Knowles Solter mouse blastocyst... 36 4.0

AA957268, AA957268 UI-R-E1-fq-e-06-0-UI.s1 UI-R-E1 Rattus nor... T00613, T00613 wEST01334 Caenorhabditis elegans cDNA clone CE... 38 0.90 AA956139, AA956139 UI-R-E1-fi-h-08-0-UI.s1 UI-R-E1 Rattus nor... 38 0.90 AA660819, AA660819 00713 MtRHE Medicago truncatula cDNA 5' 38 0.90 AA125602, AA125602 JM00M011.QM3 Miracidia Sic 3/96 Schistosom... 36 3.6 Z33974, ATTS3035 A. thaliana transcribed sequence; clone PAP... 36 3.6 C68472, C68472 C.elegans cDNA clone yk305a12:5' end, singl... 36 3.6 AA785775, AA785775 h4b05a1.fl Aspergillus nidulans 24hr asexu... Z32602, ATTS2730 A. thaliana transcribed sequence; clone PAP... AA943364, AA943364 EST198863 Normalized rat brain, Bento Soar... Z32603, ATTS2731 A. thaliana transcribed sequence; clone PAP... AA842765, AA842765 M-EST080 Sugarcane mature stalk Saccharum ... 36 3.6 D45997, RICS10346A Rice cDNA, partial sequence (S10346 1A). 36 3.6 AA955567, AA955567 UI-R-E1-fa-a-08-0-UI.s1 UI-R-E1 Rattus nor... AA800634, AA800634 EST190131 Normalized rat lung, Bento Soare... 36 3.6 AA660859, AA660859 00754 MtRHE Medicago truncatula cDNA 5' si... AA800635, AA800635 EST190132 Normalized rat lung, Bento Soare... 36 3.6 D46069, RICS10475A Rice cDNA, partial sequence (S10475 1A). 36 3.6 H32878, H32878 EST108396 Rat PC-12 cells, untreated Rattus sp...

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Z99297, HS262D12 Homo sapiens DNA sequence from PAC 262D12 o... 1963 0.0 Z81540, CEF46B3 Caenorhabditis elegans cosmid F46B3, complet... 40 0.89 U67488, U67488 Methanococcus jannaschii section 30 of 150 of ... 38 3.5 AE000786, AE000786 Borrelia burgdorferi plasmid lp28-2, compl... 38 3.5 L02053, OMMGSHTR1 Ommastrephes sloani glutathione transferase... 38 3.5 AC004521, ATAC004521 Arabidopsis thaliana chromosome II BAC F... 38 3.5 L41250, DROGPDHN Drosophila nebulosa glycerol-3-phosphate deh... 38 3.5 AE000619, HPAE000619 Helicobacter pylori section 97 of 134 of... 38 3.5 U39720, Mycoplasma genitalium ackA, licA, mucB, rpL10, rpL32... 38 3.5 AC004533, HUAC004533 Homo sapiens Chromosome 16 BAC clone CIT... 38 3.5 U62292, HSU62292 Human elastin (ELN) gene, partial cds 38 3.5

HUMAN ESTs

W02630, W02630 za52c02.r1 Soares fetal liver spleen 1NFLS Hom... 1009 0.0 AA557183, AA557183 nl74f12.s1 NCI_CGAP_Br2 Homo sapiens cDNA ... 874 0.0 AA761171, AA761171 nz09e11.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 866 0.0 AA976975, AA976975 oq26g11.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... 854 0.0 AA449515, AA449515 zx06b11.r1 Soares total fetus Nb2HF8 9w Ho... 848 0.0

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AA678392, AA678392 zi26h10.s1 Soares fetal liver spleen 1NFLS... 848 0.0 AA909198, AA909198 ol12d06.s1 Soares_NFL_T_GBC_S1 Homo sapien... 831 0.0 W79208, W79208 zd79g05.rl Soares fetal heart NbHH19W Homo sap... 813 0.0 W03125, W03125 za53c02.r1 Soares fetal liver spleen 1NFLS Hom... 807 0.0 W94750, W94750 ze13h08.rl Soares fetal heart NbHH19W Homo sap... 785 0.0 AA354894, AA354894 EST63217 Jurkat T-cells V Homo sapiens cDN... 771 0.0 H70075, H70075 yr92b03.r1 Homo sapiens cDNA clone 212717 5'. W77859, W77859 zd70b08.rl Soares fetal heart NbHH19W Homo sap... 728 0.0 AA425424, AA425424 zw48f03.s1 Soares total fetus Nb2HF8 9w Ho... 718 0.0 AA476893, AA476893 zu29f09.rl Soares ovary tumor NbHOT Homo s... 688 0.0 AA456676, AA456676 aa01h02.s1 Soares NhHMPu S1 Homo sapiens c... 688 0.0 AA662309, AA662309 nu97c11.s1 NCI_CGAP Pr22 Homo sapiens cDNA... 668 0.0 W72135, W72135 zd70b08.s1 Soares fetal heart NbHH19W Homo sap... 650 0.0 N74362, N74362 za52c02.s1 Homo sapiens cDNA clone 296162 3'. N66917, N66917 za47d09.s1 Homo sapiens cDNA clone 295697 3'. 585 e-165 AA251287, AA251287 zs04c06.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 583 e-164 AA971082, AA971082 op70h01.s1 Soares NFL T_GBC S1 Homo sapien... 567 e-160 W78165, W78165 zd79g05.s1 Soares fetal heart NbHH19W Homo sap... 565 e-159 AA253290, AA253290 zr71g03.r1 Soares NhHMPu S1 Homo sapiens c... 559 e-157 AA729063, AA729063 nw22f08.s1 NCI_CGAP_GCB0 Homo sapiens cDNA... 557 e-157 AA987313, AA987313 or81h06.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 553 e-155 AA300954, AA300954 EST13832 Testis tumor Homo sapiens cDNA 5'... 541 e-152 AA425594, AA425594 zw48f03.r1 Soares total fetus Nb2HF8 9w Ho... 529 e-148 N24014, N24014 yx87g10.s1 Homo sapiens cDNA clone 268770 3'. 523 e-146 AA947355, AA947355 od86e12.s1 NCI_CGAP Ov2 Homo sapiens cDNA ... 504 e-140 AA121074, AA121074 zl88b06.s1 Stratagene colon (#937204) Homo... 460 e-127 AA742964, AA742964 ny15d01.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 454 e-126 AA306814, AA306814 EST177885 Colon carcinoma (HCC) cell line ... 452 e-125 W87699, W87699 zh65b11.rl Soares fetal liver spleen 1NFLS S1 ... 446 e-123 W87700, W87700 zh65b11.s1 Soares fetal liver spleen 1NFLS S1 ... 438 e-121 AA449084, AA449084 zx06b11.s1 Soares total fetus Nb2HF8 9w Ho... 398 e-109 N99231, N99231 zb76f11.s1 Soares senescent fibroblasts NbHSF ... 391 e-106 N49900, N49900 yv24d04.s1 Homo sapiens cDNA clone 243655 3'. 383 e-104 AA782911, AA782911 ai62a10.s1 Soares testis NHT Homo sapiens ... 365 6e-99 AA936553, AA936553 on23g11.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 361 9e-98 N74414, N74414 za53c02.s1 Homo sapiens cDNA clone 296258 3'. 353 2e-95 AA834628, AA834628 od98a10.s1 NCI_CGAP_Ov2 Homo sapiens cDNA ... 341 8e-92 AA693756, AA693756 zi55f11.s1 Soares fetal liver spleen 1NFLS... 341 8e-92 AA909616, AA909616 ol09d06.s1 Soares_NFL_T_GBC_S1 Homo sapien... 341 8e-92 H69662, H69662 yr92b03.s1 Homo sapiens cDNA clone 212717 3'. 321 8e-86 AA249558, AA249558 jj7521.seq.F Human fetal heart, Lambda ZAP... 317 1e-84 AA911960, AA911960 oh88g08.s1 NCI_CGAP Co8 Homo sapiens cDNA ... 317 1e-84 AA969099, AA969099 op55e06.s1 Soares_NFL_T_GBC_S1 Homo sapien... 303 2e-80 AA766191, AA766191 oa12g08.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 212 5e-53 AA689312, AA689312 nx05e10.s1 NCI_CGAP_GC3 Homo sapiens cDNA ... 200 2e-49

AA418586, AA418586 zv93e05.rl Soares NhHMPu S1 Homo sapiens c... 182 5e-44 AA418570, AA418570 zv93e05.s1 Soares NhHMPu S1 Homo sapiens c... 182 5e-44 AA534939, AA534939 nf82f03.s1 NCI CGAP Co3 Homo sapiens cDNA ... 167 3e-39 AA888430, AA888430 nw74e05.s1 NCI CGAP Pr12 Homo sapiens cDNA... 167 3e-39 N50003, N50003 vv24d04.rl Homo sapiens cDNA clone 243655 5' s... 149 6e-34 AA535102, AA535102 nf84f06.s1 NCI_CGAP_Co3 Homo sapiens cDNA ... 135 1e-29 AA262335, AA262335 zr71g03.s1 Soares NhHMPu S1 Homo sapiens c... 129 6e-28 AA766681, AA766681 oa34c05.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 105 9e-21 AA761492, AA761492 nz27a05.s1 NCI CGAP GCB1 Homo sapiens cDNA... 101 1e-19 AA688350, AA688350 nv15a05.s1 NCI CGAP Pr22 Homo sapiens cDNA... 90 5e-16 AA347041, AA347041 EST53285 Fetal heart II Homo sapiens cDNA ... 76 8e-12 T94395, T94395 ye35e02.s1 Homo sapiens cDNA clone 119738 3'. 46 0.007 AA833565, AA833565 aj46a02.s1 Soares testis NHT Homo sapiens ... 46 0.007 AA095460, AA095460 14630.seq.F Fetal heart, Lambda ZAP Expres... 40 0.43 AA904415, AA904415 ok07e06.s1 Soares NFL T GBC S1 Homo sapien... 40 0.43 AI018800, AI018800 ov32h04.x1 Soares testis NHT Homo sapiens ... 38 1.7 AA631083, AA631083 nq77e07.s1 NCI CGAP Pr22 Homo sapiens cDNA... 38 1.7

AA399772, AA399772 vd70g05.rl Beddington mouse embryonic regi... 347 5e-94 AA467106, AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 309 1e-82 AI046844, AI046844 uh55c11.r1 Soares mouse embryonic stem cel... 208 3e-52 AA475075, AA475075 vh11g05.rl Soares mouse mammary gland NbMM... 194 4e-48 AA646094, AA646094 vs31e06.rl Stratagene mouse Tcell 937311 M... 186 1e-45 AA390020, AA390020 vb30e07.rl Soares mouse lymph node NbMLN M... 170 6e-41 AA245553, AA245553 my52g04.rl Barstead mouse pooled organs MP... 170 6e-41 AA930741, AA930741 vs57b02.rl Stratagene mouse skin (#937313)... 155 4e-36 W62610, W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 117 8e-25 AA239270, AA239270 my40e01.rl Barstead mouse pooled organs MP... 109 2e-22 AA015148, AA015148 mh16e01.rl Soares mouse placenta 4NbMP13.5... 54 1e-05 AA764095, AA764095 vw09h02.rl Soares 2NbMT Mus musculus cDNA ... 38 0.61 AA238570, AA238570 my35h02.rl Barstead mouse pooled organs MP... 38 0.61 AA600576, AA600576 vm75f08.rl Knowles Solter mouse blastocyst... 38 0.61 AA636273, AA636273 vq76a10.s1 Knowles Solter mouse 2 cell Mus... 36 2.4 AA051407, AA051407 mj41f08.rl Soares mouse embryo NbME13.5 14... AA823136, AA823136 vw41b03.rl Soares mouse mammary gland NbMM... W83831, W83831 mf26a06.rl Soares mouse embryo NbME13.5 14.5 M... 36 2.4 D77944, MUSC0D06 Mouse embryonal carcinoma F9 cell cDNA, C0D06 AA915408, AA915408 vz29h04.rl Soares 2NbMT Mus musculus cDNA ... 36 2.4 AI047229, AI047229 uh63a09.rl Soares mouse embryonic stem cel... 36 2.4 AA271880, AA271880 va73d01.rl Soares mouse 3NME12 5 Mus muscu... 36 2.4 AA475165, AA475165 vg95f01.rl Barstead mouse pooled organs MP... 36 2.4 AA619774, AA619774 vl58a05.s1 Knowles Solter mouse 2 cell Mus... 36 2.4

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AA673116, AA673116 vn49g11.rl Barstead mouse myotubes MPLRB5 ... 36 2.4 AA870623, AA870623 vq24a07.rl Barstead stromal cell line MPLR... 36 2.4 W58907, W58907 md52f12.rl Soares mouse embryo NbME13.5 14.5 M... 36 2.4 AA690593, AA690593 vu53d05.rl Soares mouse mammary gland NbMM... 36 2.4 AA754801, AA754801 vu21f03.rl Barstead mouse myotubes MPLRB5 ... 36 2.4 AA271607, AA271607 va72a12.rl Soares mouse 3NME12 5 Mus muscu... 36 2.4 AA064256, AA064256 mj66a03.rl Soares mouse p3NMF19.5 Mus musc... 36 2.4 AA475144, AA475144 vg95d01.rl Barstead mouse pooled organs MP... 36 2.4 AA197736, AA197736 mv02g08.rl GuayWoodford Beier mouse kidney... 36 2.4

AA817944, AA817944 UI-R-A0-ag-e-01-0-UI.s1 UI-R-A0 Rattus nor... 40 0.14 F14714, SSC8B01 S.scrofa mRNA; expressed sequence tag (5'; c... 38 0.54 H91505, H91505 SWMFCA089SK Brugia malayi microfilaria cDNA (S... 36 2.1 AA998610, AA998610 UI-R-C0-if-c-04-0-UI.s1 UI-R-C0 Rattus nor... 36 2.1 AA893562, AA893562 EST197365 Normalized rat liver, Bento Soar... 36 2.1 AI008397, AI008397 EST202848 Normalized rat embryo, Bento Soa... 36 2.1

SEQ ID NO:554

Z92544, HS313D11 Human DNA sequence from cosmid 313D11 from ... 700 0.0 Z46940, HSPRMTNP2 H.sapiens PRM1 gene, PRM2 gene and TNP2 gene 44 0.048 U85039, TMU85039 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 U85251, TMU85251 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 AF003630, AF003630 Theileria mutans clone 15, 32 kDa immunodo... 42 0.19 AF003629, AF003629 Theileria mutans clone 9, 32 kDa immunodom... 42 0.19 AB007884, AB007884 Homo sapiens KIAA0424 mRNA, partial cds 42 0.19 U85040, TMU85040 Theileria mutans 32 kDa immunodominant pirop... 42 0.19 Z97343, ATFCA8 Arabidopsis thaliana DNA chromosome 4, ESSA I... 40 0.75 L19655, TOSRNA1X Tomato ringspot virus polyprotein (RNA-1) ge... 40 0.75 M73822, TOSRNA1A Tomato ringspot virus RNA1 gene, 5' end. 40 0.75 L02543, BOVMTNNT Bos taurus nicotinamide nucleotide transhydr... 40 0.75 J03534, BOVNAD Bovine mitochondrial nicotinamide nucleotide t... 40 0.75 M62862, TRBRTE Trypanosoma cruzi retrotransposon encoding gag... X72711, MMREPCFC M.musculus mRNA for replication factor C, l... M88489, MUSNBP Mus musculus nonamer binding protein mRNA, com... U36441, MMU36441 Mus musculus differentiation specific elemen... 38 3.0 AB002354, AB002354 Human mRNA for KIAA0356 gene, complete cds J03149, CATFMSC Cat (F.domesticus) c-fms proto-oncogene mRNA ... 38 3.0 J05475, CHKVICOLL Chicken type VI collagen alpha 2 (VI) subun... 38 3.0

AF038163, AF038163 Homo sapiens interleukin-15 (IL-15) gene, ... 38 3.0 X75917, HSFBMBF H.sapiens mRNA for fetal beta-MHC binding fa... 38 3.0 X06542, DMHSPG3 Drosophila heat shock gene 3 from 67B locus 38 3.0 D17315, DRODAGK Fruit fly mRNA for diacylglycerol kinase, co... 38 3.0 Z58600, HS45E3F H.sapiens CpG DNA, clone 45e3, forward read ... 38 3.0 D78638, D78638 Xenopus laevis mRNA for DNA (cytosine-5-)-met... 38 3.0 Z49204, MMNADPTRH M.musculus mRNA for NADP transhydrogenase. 38 3.0 L10425, BPEMETC Bordetella avium beta-cystathionase-lyase (me... 38 3.0 U01222, U01222 Mus musculus activator 1 large subunit (A1-p14... 38 3.0 U15037, MMU15037 Mus musculus replication factor C large subu... 38 3.0 K01643, FCSSMONC Feline sarcoma virus (McDonough strain) tran... 38 3.0 Z57538, HS183C6F H.sapiens CpG DNA, clone 183c6, forward rea... 38 3.0 U07157, MMU07157 Mus musculus ISRE-binding protein (IBF-1) mR... 38 3.0 Z64961, HS183F7R H.sapiens CpG DNA, clone 183f7, reverse rea... 38 3.0

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SEQ ID NO:555

AF039693, AF039693 Homo sapiens unknown protein mRNA, complet... 916 0.0 S51239, S51239 calreticulin [Aplysia californica=marine snail... 48 0.005 Z74035, CEF47G9 Caenorhabditis elegans cosmid F47G9, complet... AF022814, AF022814 Fugu rubripes transcription factor (SLP-1)... 44 0.073 X82638, CSCYTOX C.sordelii cytotoxin gene U63063, SCU63063 Saccharomyces cerevisiae something about sil... 42 0.29 X63501, SCRPC53 S.cerevisiae RPC53 gene for RNA polymerase C... U67572, U67572 Methanococcus jannaschii section 114 of 150 of... 42 0.29 Z74201, SCYDL153C S.cerevisiae chromosome IV reading frame O... 42 0.29 U66032, MTU66032 Methanosarcina thermophila CO dehydrogenase/... 42 0.29 Z95620, SPBC3D6 S.pombe chromosome II cosmid c3D6 42 0.29 X97751, SCIV23 S.cerevisiae chrIV genes STE7, CLB3, MSH5, RP... 42 0.29 X65541, ATCAN A.thaliana mRNA for carbonic anhydrase 42 0.29 L14750, ATHCARANHY Arabidopsis thaliana carbonic anhydrase ge... 42 0.29 U00995, U00995 Rattus norvegicus TA1 mRNA, complete cds. 40 1.1 S73876, S73876 FPR3=FKBP-70 [Saccharomyces cerevisiae, Genomi... 40 1.1 U12825, SCU12825 Saccharomyces cerevisiae transcription facto... 40 1.1 Z74237, SCYDL189W S.cerevisiae chromosome IV reading frame O... 40 1.1 U76906, REU76906 Rhizobium etli FixK (fixK), FixN (fixN), mon... 40 1.1

AF050157, MMHC135G15 Mus musculus major histocompatibility lo... 40 1.1 X58857, SCPPH22 S.cerevisiae PPH22 gene for protein phosphat... 40 1.1 X79379, SCPROIS S. cerevisiae gene for proline isomerase 40 1.1 Z68341, CEF01G4 Caenorhabditis elegans cosmid F01G4, complet... 40 1.1 M17192, MUSHOX1 Mouse homeodomain protein (Hox1.1) mRNA, comp... 40 1.1 U50307, CELF43H9 Caenorhabditis elegans cosmid F43H9. 40 1.1 S73144, S73144 bone sialoprotein [cattle, fetal bone cells, m... 40 1.1 L34569, YSCFPR3A Saccharomyces cerevisiae (clone pBYNG1) prol... D78303, D78303 Rattus norvegicus YT521 mRNA for RNA splicing... X83276, SCDNAIV S.cerevisiae DNA for ORFs from chromosome IV 40 1.1 U54558, HSU54558 Human translation initiation factor eIF3 p66... Z50109, CEC09H10 Caenorhabditis elegans cosmid C09H10, compl... 40 1.1 X56983, EAVATP1 E.arvense gene for catalytic 70kDa V-ATPase ... 40 1.1 AB011125, AB011125 Homo sapiens mRNA for KIAA0553 protein, p... 40 1.1 Z46373, SC8248 S.cerevisiae chromosome XIII cosmid 8248 40 1.1 AF039042, CELZK697 Caenorhabditis elegans cosmid ZK697 40 1.1 Z28028, SCYKL028W S.cerevisiae chromosome XI reading frame O... 40 1.1 AC005266, AC005266 Homo sapiens chromosome 19, cosmid F23465... U60822, HSU60822 Human dystrophin (DMD) gene, exons 7, 8 and ... 38 4.5 AJ003141, HVAJ3141 Hordeum vulgare mRNA for stress-related p... M26250, CRAGAP43 Goldfish (C.auratus) growth-associated prote... X95267, GGRYR3 G.gallus mRNA for ryanodine receptor type 3 38 4.5 L37092, MUSCDPK Mus musculus cyclin-dependent kinase homologu... 38 4.5 Z72507, CEF17C11 Caenorhabditis elegans cosmid F17C11, compl... 38 4.5 U29608, DMU29608 Drosophila melanogaster large tumor suppress... 38 4.5 Z49072, CET24A11 Caenorhabditis elegans cosmid T24A11, compl... 38 4.5 M83142, RATBGASTR Rattus norvegicus beta-galactoside-alpha 2,... 38 4.5 Z20656, HSCAMHCA Homo sapiens of cardiac alpha-myosin heavy ... M82937, YSACS2A Candida albicans chitin synthase 2 (CHS2) gen... U28888, MMU28888 Mus musculus neurogenic differentiation fact... S66408, S66408 c-erbB=proto-oncogene {exon 1, promoter} [chic... AC002396, AC002396 Arabidopsis thaliana chromosome I BAC F3I6... 38 4.5 AE000665, MMAE000665 Mus musculus TCR beta locus from bases 5... L39837, DROWARTS Drosophila melanogaster tumor supressor (war... 38 4.5 AG000377, AG000377 Homo sapiens genomic DNA, 21q region, clo... X05632, HSMHCAG1 Human alpha-MHC gene for myosin heavy chain... AC002108, AC002108 Genomic sequence from Mouse 4, complete se... U37219, HSU37219 Human cyclophilin-like protein CyP-60 mRNA, ... M58633, MUSP58GTA Mouse p58/GTA protein kinase mRNA, complete... 38 4.5 M25162, HUMMYHC08 Human cardiac alpha-myosin heavy chain (MYH... Z46259, SCRPD3COS S.cerevisiae FY1676 RPD3 gene. 38 4.5 U09558, LJU09558 Lactobacillus johnsonii ATCC 11506 insertion... 38 4.5 U66160, MMUSC104 Mus musculus extracellular matrix associated... 38 4.5 Z73126, SCYLL021W S.cerevisiae chromosome XII reading frame ... U83981, HSU83981 Homo sapiens apoptosis associated protein (G... 38 4.5

U59897, MRU59897 Macropus robustus hypoxanthine phosphoribosy 38 4.5
D38256, YSCSCT1 Yeast gene for suppressor of ctr mutation 38 4.5
X69838, HSG9A H.sapiens mRNA for G9a 38 4.5
X52952, RNCMOSO Rat mRNA for c-mos 38 4.5
U37221, HSU37221 Human cyclophilin-like protein mRNA, partial 38 4.5
X65880, DPRH4OP1 D.pseudoobscura rh4 opsin gene, exon 1 38 4.5
U58971, NTU58971 Nicotiana tabacum calmodulin-binding protein 38 4.5
Z35773, SCYBL012C S.cerevisiae chromosome II reading frame O 38 4.5
X67668, MMHMG2 M.musculus mRNA for high mobility group 2 pro 38 4.5
L81727, HSL81727 Homo sapiens (subclone 1_d5 from P1 H69) DNA 38 4.5
AL023800, HS833B2 Human DNA sequence *** SEQUENCING IN PROGR 38 4.5
X62438, HVPERO H.vulgare mRNA for peroxidase 38 4.5
AC004096, AC004096 Mouse Cosmid ma66a100 from 14D1-D2, comple 38 4.5
AL008980, PFSC03050 Plasmodium falciparum DNA *** SEQUENCING 38 4.5
U64827, MMU64827 Mus musculus extracellular matrix associated 38 4.5
AC003010, HUAC003010 Homo sapiens Chromosome 16 BAC clone CIT 38 4.5
AE001002, AE001002 Archaeoglobus fulgidus section 105 of 172 38 4.5
U86662, LEU86662 Lycopersicon esculentum VPS41 (tVPS41) mRNA, 38 4.5
M20386, CHKEGFR Chicken epidermal growth factor receptor (CER 38 4.5
M77637, CHKEGF Gallus gallus EGF/TGF-alpha receptor (c-erbB) 38 4.5
U08185, MMU08185 Mus musculus BALB/c zinc-finger protein Blim 38 4.5
AC004231, AC004231 Homo sapiens chromosome 17, clone hRPC.111 38 4.5
Z50100, HVC39SAT H.vulgare GAA-satellite DNA 38 4.5
X53731, SCSPA2G S. cerevisiae SPA2 gene 38 4.5
U37220, HSU37220 Human cyclophilin-like protein mRNA, partial 38 4.5
X97560, SC32KBF S.cerevisiae 32kb DNA fragment of chromosome 38 4.5
AB011479, AB011479 Arabidopsis thaliana genomic DNA, chromos 38 4.5
U89340, LVU89340 Lytechinus variegtus Endo16 homolog (LvEndo1 38 4.5
U73850, TCU73850 Trypanosoma cruzi 29 kDa proteasome subunit 38 4.5
AB006698, AB006698 Arabidopsis thaliana genomic DNA, chromos 38 4.5
D37888, CYIMYC2 Cyprinus carpio c-myc gene for c-Myc, comple 38 4.5
AF017349, MMDSGIII 7 Mus musculus desmoglein 3 (Dsg3) gene, i 38 4.5
X91807, OSTA136 O.sativa mRNA for alpha-tubulin (clone OSTA 38 4.5
Z71587, SCYNL311C S.cerevisiae chromosome XIV reading frame 38 4.5
AE000742, AE000742 Aguifex aeolicus section 74 of 109 of the 38 4.5

HUMAN ESTs

AA324311, AA324311 EST27136 Cerebellum II Homo sapiens cDNA 5... 593 e-167 AA639190, AA639190 ns04a01.rl NCI_CGAP_Ew1 Homo sapiens cDNA ... 513 e-143 AA172199, AA172199 zo96a06.rl Stratagene ovarian cancer (#937... 505 e-141 AA588066, AA588066 nk10d08.sl NCI_CGAP_Co2 Homo sapiens cDNA ... 502 e-140 AA412036, AA412036 zt68d09.sl Soares testis NHT Homo sapiens ... 502 e-140 AA508745, AA508745 ni23a03.sl NCI_CGAP_Co4 Homo sapiens cDNA ... 502 e-140

AA480337, AA480337 ne33a03.s1 NCI CGAP Co3 Homo sapiens cDNA ... 502 e-140 AA902270, AA902270 ok69e04.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... 502 e-140 AA947303, AA947303 ok20d04.s1 Soares_NSF_F8_9W_OT_PA_P_S1 Hom... 502 e-140 R23642, R23642 yh35e03.r1 Homo sapiens cDNA clone 131740 5'. 490 e-136 AA811913, AA811913 ob51d06.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 464 e-128 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 464 e-128 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 400 e-109 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. AA402403, AA402403 zt68d09.rl Soares testis NHT Homo sapiens ... 315 6e-84 R58372, R58372 G3243 Fetal heart Homo sapiens cDNA clone G324... 262 8e-68 AA389703, AA389703 M421 Fetal heart, Lambda ZAP Express Homo ... 202 6e-50 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 4e-20 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 1e-08 T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.14 AA179601, AA179601 zp49f10.r1 Stratagene HeLa cell s3 937216 ... 42 0.14 AA928679, AA928679 on48e08.s1 NCI_CGAP_Co8 Homo sapiens cDNA ... 40 0.55 AA887972, AA887972 nq95g11.s1 NCI CGAP Co10 Homo sapiens cDNA... W46946, W46946 zc40c05.s1 Soares senescent fibroblasts NbHSF ... 40 0.55 AA887862, AA887862 nq99b08.s1 NCI_CGAP Co10 Homo sapiens cDNA... 40 0.55 AA554819, AA554819 ni34d08.s1 NCI CGAP Lu1 Homo sapiens cDNA ... 40 0.55 AA557362, AA557362 nl81d12.s1 NCI CGAP Br2 Homo sapiens cDNA ... 40 0.55 AA252258, AA252258 zr29e04.s1 Stratagene NT2 neuronal precurs... 40 0.55 N34310, N34310 yy52b10.s1 Homo sapiens cDNA clone 277147 3' s... 40 0.55 AA552228, AA552228 nk06b04.s1 NCI_CGAP_Co2 Homo sapiens cDNA ... 40 0.55 AI017648, AI017648 ou99b02.x1 NCI_CGAP Kid3 Homo sapiens cDNA... 40 0.55 T17395, T17395 NIB846 Normalized infant brain, Bento Soares H... 40 0.55 AA219659, AA219659 zr05e10.s1 Stratagene NT2 neuronal precurs... AA463841, AA463841 zx67f06.r1 Soares total fetus Nb2HF8 9w Ho... N66817, N66817 za09b11.s1 Homo sapiens cDNA clone 292029 3' s... AA167358, AA167358 zp06f12.s1 Stratagene ovarian cancer (#937... 40 0.55 AA063505, AA063505 zf70d02.rl Soares pineal gland N3HPG Homo ... 40 0.55 AA731625, AA731625 nw64a04.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... AA100119, AA100119 zl80g04.s1 Stratagene colon (#937204) Homo... AA181572, AA181572 zp51d04.s1 Stratagene HeLa cell s3 937216 ... 40 0.55 AA327182, AA327182 EST30459 Colon I Homo sapiens cDNA 5' end ... 40 0.55 R48608, R48608 yj65f07.s1 Homo sapiens cDNA clone 153637 3' s... 40 0.55 AA678485, AA678485 ah06e04.s1 Gessler Wilms tumor Homo sapien... 40 0.55 AA082353, AA082353 zn38c11.rl Stratagene endothelial cell 937... 40 0.55 AA633213, AA633213 nq57c06.s1 NCI CGAP Co9 Homo sapiens cDNA ... 40 0.55 W38410, W38410 zc77g09.s1 Pancreatic Islet Homo sapiens cDNA ... 40 0.55 AA345893, AA345893 EST51967 Gall bladder I Homo sapiens cDNA ... N26876, N26876 yx97f06.s1 Homo sapiens cDNA clone 269699 3' s... N95279, N95279 zb60c09.s1 Soares fetal lung NbHL19W Homo sapi... AI041637, AI041637 ox92h08.x1 Soares_senescent_fibroblasts_Nb... 40 0.55 N67830, N67830 za05d12.s1 Homo sapiens cDNA clone 291671 3' s...

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AA563402, AA563402 vl75d08.rl Knowles Solter mouse blastocyst...
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AA097645, AA097645 mm36f09.r1 Stratagene mouse skin (#937313)... 38 0.78
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AA122581, AA122581 mn25c08.rl Beddington mouse embryonic regi... 38 0.78
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AA200881, AA200881 mu03c09.rl Soares mouse 3NbMS Mus musculus...
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AA208446, AA208446 mv85e01.rl GuayWoodford Beier mouse kidney... 36 3.1
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AA267119, AA267119 mz74d07.rl Soares mouse lymph node NbMLN M...
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AI006122, AI006122 ua86h01.rl Soares mouse mammary gland NbMM... 36 3.1
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W77413, W77413 me64d06.r1 Soares mouse embryo NbME13.5 14.5 M...
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W62181, W62181 md87d08.rl Soares mouse embryo NbME13.5 14.5 M...
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AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu...
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AA212823, AA212823 mw81c07.rl Soares mouse NML Mus musculus c... 36 3.1
AA125061, AA125061 mq83d10.r1 Stratagene mouse melanoma (#937...
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AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... 44 0.011

AA520185, AA520185 TgESTzz39d03.s1 TgME49 invivo Bradyzoite c... 44 0.011 AA531917, AA531917 TgESTzz48f01.rl TgME49 invivo Bradyzoite c... 44 0.011 AA519997, AA519997 TgESTzz36h03.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA520811, AA520811 TgESTzz64d05.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA520866, AA520866 TgESTzz68e05.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA519844, AA519844 TgESTzz36c03.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA274295, AA274295 TgESTzz24c11.s1 TgME49 invivo Bradyzoite c... 44 0.011 AA520901, AA520901 TgESTzz65a05.r1 TgME49 invivo Bradyzoite c... 44 0.011 AA519829, AA519829 TgESTzz36a02.rl TgME49 invivo Bradyzoite c... 44 0.011 AA531839, AA531839 TgESTzz47h05.r1 TgME49 invivo Bradyzoite c... 44 0.011 C70525, C70525 C.elegans cDNA clone yk409g6: 5' end, single... 44 0.011 AA520235, AA520235 TgESTzz53c06.r1 TgME49 invivo Bradyzoite c... 42 0.044 T42800, T42800 6063 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 42 0.044 R29976, R29976 12581 Lambda-PRL2 Arabidopsis thaliana cDNA cl... H32045, H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 40 0.18 AA819924, AA819924 MF5MA171.AE3 S. mansoni female adult Lambd... H37128, H37128 15257 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 40 0.18 T04367, T04367, 414 Lambda-PRL2 Arabidopsis thaliana cDNA clon... 40 0.18 R90528, R90528 16883 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 40 0.18 AA660422, AA660422 00298 MtRHE Medicago truncatula cDNA 5' 40 0.18 U94861, RRU94861 Rattus norvegicus clone HCY3 mRNA sequence 40 0.18 F14275, ATTS5197 A. thaliana transcribed sequence; clone YBY... 38 0.69 W43730, W43730 23107 CD4-16 Arabidopsis thaliana cDNA clone H... N65025, N65025 20065 Lambda-PRL2 Arabidopsis thaliana cDNA cl... AI001628, AI001628 EST0210 Tilapia brain cDNA library in pUC1... 38 0.69 H74687, H74687 383 Brassica napus cDNA clone R25R. 38 0.69 AA395597, AA395597 27394 Lambda-PRL2 Arabidopsis thaliana cDN... 38 0.69 AA753070, AA753070 97AS2091 Rice Immature Seed Lambda ZAPII c... 38 0.69 D41274, RICS3647A Rice cDNA, partial sequence (S3647 1A). 38 0.69 Z25731, ATTS1208 A. thaliana transcribed sequence; clone VCV... 38 0.69 N82780, N82780 TgESTzy34e03.rl TgRH Tachyzoite cDNA Toxoplasm... 38 0.69 AA597822, AA597822 29889 Lambda-PRL2 Arabidopsis thaliana cDN... 38 0.69 AA948906, AA948906 LD27590.5prime LD Drosophila melanogaster ... 38 0.69 AI013695, AI013695 EST208370 Normalized rat spleen, Bento Soa... 38 0.69 AA753263, AA753263 96BS0294 Rice Immature Seed Lambda ZAPII c... 38 0.69 F14402, ATTS5324 A. thaliana transcribed sequence; clone TAP... 36 2.7 T46158, T46158 9421 Lambda-PRL2 Arabidopsis thaliana cDNA clo... C91400, C91400 Dictyostelium discoideum slug cDNA, clone SSK169 T46009, T46009 9272 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AA440655, AA440655 LD15510.5prime LD Drosophila melanogaster ... AA559374, AA559374 MU002092.NH3 York-Harrop-lung-A Schistosom... Z32623, ATTS2751 A. thaliana transcribed sequence; clone YAP... 36 2.7 T43683, T43683 6946 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AA263535, AA263535 LD06645.5prime LD Drosophila melanogaster ... C37095, C37095 C.elegans cDNA clone yk482c11: 3' end, singl... 36 2.7

C57017, C57017 C.elegans cDNA clone yk308h9: 3' end, single... C93857, C93857 Dictyostelium discoideum slug cDNA, clone SSL794 C92242, C92242 Dictyostelium discoideum slug cDNA, clone SSD283 36 2.7 Z33976, ATTS3037 A. thaliana transcribed sequence; clone YAP... 36 2.7 R62091, R62091 EST351 Strongylocentrotus purpuratus cDNA 5' end. 36 2.7 AA567455, AA567455 HL01288.5prime HL Drosophila melanogaster ... 36 2.7 C74456, C74456 Rice cDNA, partial sequence (E31357 1A) AA753227, AA753227 97AS2316 Rice Immature Seed Lambda ZAPII c... 36 2.7 C92456, C92456 Dictyostelium discoideum slug cDNA, clone SSE569 T20458, T20458 2466 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 R29905, R29905 12510 Lambda-PRL2 Arabidopsis thaliana cDNA cl... M79841, M79841 wEST00378 Caenorhabditis elegans cDNA clone CE... 36 2.7 Z17562, ATTS0136 A. thaliana transcribed sequence; clone TAT... 36 2.7 D71983, CELK084H2R C.elegans cDNA clone yk84h2: 3' end, sin... T20404, T20404 2412 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 2.7 AI012789, AI012789 EST207240 Normalized rat placenta, Bento S... 36 2.7 U83048, BTU83048 Bos taurus clone 0429 mRNA sequence 36 2.7 AA660182, AA660182 00022 MtRHE Medicago truncatula cDNA 5' si... 36 2.7 D48514, RICS14740A Rice cDNA, partial sequence (S14740 1A). 36 2.7 C90110, C90110 Dictyostelium discoideum slug cDNA, clone SSI103 36 2.7 H36880, H36880 15009 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 2.7 AA699152, AA699152 HL07807.5prime HL Drosophila melanogaster ... 36 2.7 C11922, C11922 C.elegans cDNA clone yk144a11: 5' end, singl... 36 2.7 AA816691, AA816691 LD03795.5prime LD Drosophila melanogaster ... 36 2.7

SEQ ID NO:556

X99668, MM22A3 M.musculus mRNA for exon from unknown gene 22A3 260 5e-67 Z83760, CICOS41 Ciona intestinalis DNA sequence from cosmid ... 40 0.94 Z75710, CED1081 Caenorhabditis elegans cosmid D1081, complet... 40 0.94 U73628, HSU73628 Human chromosome 11 101h11 cosmid, complete ... 40 0.94 X99757, DMDYDTRO D.melanogaster mRNA for dystrophin 38 3.7 U51189, HIVU51189 HIV-1 clone 93th253 from Thailand, complete... 38 3.7 AC004118, AC004118 Drosophila melanogaster (P1 DS06238 (D26))... 38 3.7 U50313, CELF44C4 Caenorhabditis elegans cosmid F44C4. AC004503, AC004503 Homo sapiens chromosome 5, P1 clone 1354A7... 38 3.7 M16840, WHTCPCA2 Wheat Asp-tRNA gene. 38 3.7 Y13381, RNAMPH1 Rattus norvegicus mRNA for amphiphysin, amphl 38 3.7 AC002994, AC002994 Homo sapiens chromosome 17, clone HRPC987K... 38 3.7 AB008271, AB008271 Arabidopsis thaliana genomic DNA, chromos... D49701, ASNNIAD Aspergillus oryzae niaD gene for nitrate red...

 X59422, HSPLD1 H.sapiens Pl d1 repetitive DNA 38 3.7
Z98555, PFSC03027 Plasmodium falciparum DNA *** SEQUENCING I... 38 3.7

HUMAN ESTs

AA315671, AA315671 EST187451 Colon carcinoma (HCC) cell line ... 932 0.0 U56653, HSU56653 Human heat shock inducible mRNA 769 0.0 AA487685, AA487685 ab23b09.r1 Stratagene lung (#937210) Homo ... 751 0.0 AA044797, AA044797 zk67g12.rl Soares pregnant uterus NbHPU Ho... 749 0.0 AA314922, AA314922 EST186735 HCC cell line (matastasis to liv... 698 0.0 AA082278, AA082278 zn42d12.r1 Stratagene endothelial cell 937... 668 0.0 H22613, H22613 yn64f03.r1 Homo sapiens cDNA clone 173213 5'. 624 e-177 AA044743, AA044743 zk67g12.s1 Soares pregnant uterus NbHPU Ho... 622 e-176 AA487470, AA487470 ab23b09.s1 Stratagene lung (#937210) Homo ... 601 e-170 AA121057, AA121057 zm22b03.rl Stratagene pancreas (#937208) H... 581 e-164 AA194396, AA194396 zq05g05.s1 Stratagene muscle 937209 Homo s... 535 e-150 AA384283, AA384283 EST97787 Thyroid Homo sapiens cDNA 5' end AA669015, AA669015 ab88f01.s1 Stratagene lung (#937210) Homo ... 535 e-150 AA194336, AA194336 zq05g05.r1 Stratagene muscle 937209 Homo s... 505 e-141 R96173, R96173 yt84e09.r1 Homo sapiens cDNA clone 231016 5'. AA028934, AA028934 zk08b09.s1 Soares pregnant uterus NbHPU Ho... 484 e-134 AA564849, AA564849 nj22c04.s1 NCI CGAP AA1 Homo sapiens cDNA ... 442 e-122 AA932576, AA932576 oo57g10.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 440 e-121 AA876265, AA876265 oi12g09.s1 NCI CGAP GC4 Homo sapiens cDNA ... 434 e-120 AA025525, AA025525 ze86a11.s1 Soares fetal heart NbHH19W Homo... 430 e-118 U56654, HSU56654 Human heat shock inducible mRNA 426 e-117 AA746600, AA746600 nx18c02.s1 NCI CGAP GC3 Homo sapiens cDNA ... 406 e-111 AA876346, AA876346 oj24a11.s1 NCI CGAP Kid5 Homo sapiens cDNA... 406 e-111 W23082, W23082 78D1 Human retina cDNA Tsp509I-cleaved sublibr... 402 e-110 AI034059, AI034059 ow14h11.x1 Soares parathyroid tumor NbHPA ... 357 2e-96 AA662934, AA662934 nu92d09.s1 NCI CGAP Pr22 Homo sapiens cDNA... 323 2e-86 AA844331, AA844331 ai95f01.s1 Soares parathyroid tumor NbHPA ... 301 8e-80 AA249866, AA249866 y0761.seq.F Human fetal heart, Lambda ZAP ... 297 1e-78 R19215, R19215 yg24b07.rl Homo sapiens cDNA clone 33126 5'. 280 3e-73 T39355, T39355 ya04g08.rl Homo sapiens cDNA clone 60542 5'. 254 2e-65 AA731264, AA731264 nw57c08.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 220 2e-55 AA768549, AA768549 oa67c07.s1 NCI CGAP GCB1 Homo sapiens cDNA... 220 2e-55 AA668506, AA668506 ac49a11.s1 Stratagene hNT neuron (#937233)... 216 4e-54 T55337, T55337 yb79b05.s1 Homo sapiens cDNA clone 77361 3'. 198 8e-49 AA860575, AA860575 aj86a09.s1 Soares parathyroid tumor NbHPA ... 198 8e-49 AA335548, AA335548 EST39962 Epididymus Homo sapiens cDNA 5' end 109 6e-22 R13183, R13183 yf73f02.r1 Homo sapiens cDNA clone 27960 5'. 58 2e-06 T80034, T80034 yd04c06.rl Homo sapiens cDNA clone 24672 5'. 38 1.8 AA595230, AA595230 nl84g02.sl NCI_CGAP_Br2 Homo sapiens cDNA ... 38 1.8

AA871935, AA871935 vq42h02.rl Barstead bowel MPLRB9 Mus muscu... 664 0.0 AA062330, AA062330 ml35e10.rl Stratagene mouse testis (#93730... 589 e-167 AI048164, AI048164 ud71b09.y1 Sugano mouse liver mlia Mus mus... 537 e-151 W08037, W08037 mb37h01.r1 Soares mouse p3NMF19.5 Mus musculus... 462 e-128 AA387311, AA387311 vc19a03.r1 Ko mouse embryo 11 5dpc Mus mus... 264 6e-69 AA163072, AA163072 ms31a11.r1 Stratagene mouse skin (#937313)... 212 2e-53 AA596763, AA596763 vm60a10.rl Stratagene mouse Tcell 937311 M... 178 3e-43 AA562549, AA562549 vl63a11.rl Knowles Solter mouse blastocyst... 143 2e-32 AA212378, AA212378 mu44c03.r1 Soares 2NbMT Mus musculus cDNA ... 113 1e-23 AA450862, AA450862 vg55h12.rl Beddington mouse embryonic regi... 111 5e-23 AA990073, AA990073 ua59a01.r1 Soares 2NbMT Mus musculus cDNA ... 86 3e-15 AA921175, AA921175 vy54b10.rl Stratagene mouse lung 937302 Mu... 78 8e-13 AA261119, AA261119 mz89e01.rl Soares mouse NML Mus musculus c... AI005952, AI005952 ua80f06.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.6 AA123274, AA123274 mn23a08.rl Beddington mouse embryonic regi... AI036828, AI036828 vw96c02.r1 Stratagene mouse skin (#937313)... 36 2.6

H35787, H35787 EST109178 Rat PC-12 cells, NGF-treated (9 days... 105 3e-21 AA686082, AA686082 EST109179 Rat PC-12 cells, NGF-treated (9 ... 86 3e-15 C23464, C23464 Jpanese flounder liver cDNA, LE5(10) 72 4e-11 C23465, C23465 Jpanese flounder liver cDNA, LE5(10) 56 2e-06 AA520314, AA520314 TgESTzz38h12.r1 TgME49 invivo Bradyzoite c... 38 0.57 AA520085, AA520085 TgESTzz37g05.r1 TgME49 invivo Bradyzoite c... AA520033, AA520033 TgESTzz36f10.r1 TgME49 invivo Bradyzoite c... AA012516, AA012516 TgESTzz23f04.r1 TgME49cDNA Toxoplasma gond... AA274286, AA274286 TgESTzz24c01.s1 TgME49 invivo Bradyzoite c... 38 0.57 AA660585, AA660585 00471 MtRHE Medicago truncatula cDNA 5' si... 38 0.57 L35828, BNAESTBD Brassica rapa (clone F0621) expressed sequen... 38 0.57 AA520070, AA520070 TgESTzz37e05.r1 TgME49 invivo Bradyzoite c... C30080, C30080 C.elegans cDNA clone vk236c3: 3' end, single... C39044, C39044 C.elegans cDNA clone yk505a4 : 3' end, single... C55023, C55023 C.elegans cDNA clone yk422a3: 3' end, single... 36 2.3 AA542589, AA542589 fa08d06.s1 Zebrafish ICRFzfls Danio rerio ... N25370, N25370 EST000480 Schistosoma mansoni cDNA clone SMTBA... 36 2.3 AA820625, AA820625 LD24443.5prime LD Drosophila melanogaster ... AA494922, AA494922 fa12g10.rl Zebrafish ICRFzfls Danio rerio ... 36 2.3 AA495181, AA495181 fa04d06.s1 Zebrafish ICRFzfls Danio rerio ... D73287, CELK116G6R C.elegans cDNA clone yk116g6: 3' end, si... 36 2.3 C28238, C28238 Rice cDNA, partial sequence (C60429 1A) 36 2.3

SEQ ID NO:557

AF039693, AF039693 Homo sapiens unknown protein mRNA, complet... 948 0.0 S51239, S51239 calreticulin [Aplysia californica=marine snail... Z74035, CEF47G9 Caenorhabditis elegans cosmid F47G9, complet... U25723, CPU25723 Cavia porcellus alpha-2B adrenoceptor gene, ... 44 0.047 AL021407, HS13D10 Homo sapiens DNA sequence from PAC 13D10 o... 42 0.19 U67572, U67572 Methanococcus jannaschii section 114 of 150 of... 42 0.19 V01470, ZMZE01 Zea mays gene encoding a zein gene (clone lam... 42 0.19 U06631, HSU06631 Human (H326) mRNA, complete cds. 42 0.19 X82638, CSCYTOX C.sordelii cytotoxin gene 42 0.19 AE000926, AE000926 Methanobacterium thermoautotrophicum from ... AC004135, AC004135 Genomic sequence for Arabidopsis thaliana ... 42 0.19 AC003010, HUAC003010 Homo sapiens Chromosome 16 BAC clone CIT... AF050157, MMHC135G15 Mus musculus major histocompatibility lo... 40 0.74 AC002352, AC002352 Homo sapiens 12q24 PAC P256D10 complete se... X07699, MMNUCLEO Mouse nucleolin gene 40 0.74 X02399, MMHOM6 Mouse embryonal carcinoma DNA fragment contai... 40 0.74 M93661, RATNOTCHX Rat notch 2 mRNA. M17440, MUSMHC4H2S Mouse MHC (H-2) S region complement compon... U15972, MMU15972 Mus musculus homeobox (Hoxa7) gene, complete... AB001601, AB001601 Homo sapiens DBP2 mRNA for ATP-dependent ... 40 0.74 U09820, HSU09820 Human helicase II (RAD54L) mRNA, complete cds. 40 0.74 AB011149, AB011149 Homo sapiens mRNA for KIAA0577 protein, c... U26259, MMU26259 Mus musculus C2-H2 zinc finger protein mRNA.... L48363, MUSZFPTR Mus musculus zinc finger protein gene, compl... 40 0.74 AC003113, AC003113 Arabidopsis thaliana BAC F24O1 chromosome ... 40 0.74 D76432, D76432 Mouse mRNA for transcriptional repressor delt... 40 0.74 U72937, HSU72937 Human putative DNA dependent ATPase and heli... U72915, HSATRX16 Human putative DNA dependent ATPase and heli... 40 0.74 U00995, U00995 Rattus norvegicus TA1 mRNA, complete cds. 40 0.74 Z48618, SCCHVII35 S.cerevisiae genes for RAD54, ACE1(CUP2), ... 40 0.74 U75653, HSU75653 Human zinc finger helicase (Znf-HX) mRNA, co... Z72672, SCYGL150C S.cerevisiae chromosome VII reading frame ... 40 0.74 Z50109, CEC09H10 Caenorhabditis elegans cosmid C09H10, compl... 40 0.74 AF013969, AF013969 Mus musculus antigen containing epitope to... 40 0.74 M95627, HUMAAMP1X Homo sapiens angio-associated migratory cel... 40 0.74 U72936, HSU72936 Human putative DNA dependent ATPase and heli... M88753, DROHTCHRPI Fruitfly heterochromatin protein-1 gene, c... 40 0.74 U76906, REU76906 Rhizobium etli FixK (fixK), FixN (fixN), mon... 40 0.74 U97085, HSXNP14 Homo sapiens X-linked nuclear protein (ATRX) ... 40 0.74 L34363, HUMNUCPRO Human X-linked nuclear protein (XNP) gene, ... U72938, HSU72938 Human putative DNA dependent ATPase and heli...

X56983, EAVATP1 E.arvense gene for catalytic 70kDa V-ATPase ... U88539, MMU88539 Mus musculus chromatin structural protein ho... 40 0.74 U07704, HSU07704 Human protein kinase PITSLRE isoform PBETA21... U07705, HSU07705 Human protein kinase PITSLRE isoform PBETA22... 38 2.9 AF019612, AF019612 Homo sapiens S2P mRNA, complete cds 38 2.9 U04818, HSU04818 Human protein kinase PITSLRE alpha 2-4 mRNA,... 38 2.9 AB002381, AB002381 Human mRNA for KIAA0383 gene, partial cds AB009520, AB009520 Pyrococcus horikoshii OT3 genomic DNA, 13... 38 2.9 Z83848, HS57A13 Human DNA sequence from PAC 57A13 between ma... AC004592, AC004592 Homo sapiens PAC clone DJ0244J05 from 5q31... L11710, ZEFZCMYC Brachydanio rerio c-myc oncoprotein mRNA, co... D43920, CHKMETASE Chicken mRNA for DNA (cytosine-5-)-methylt... 38 2.9 U49056, RNU49056 Rattus norvegicus CTD-binding SR-like protei... 38 2.9 U04824, HSU04824 Human protein kinase PITSLRE alpha 2-1 mRNA,... U78045, HSU78045 Human collagenase and stromelysin genes, com... 38 2.9 U04816, HSU04816 Human protein kinase PITSLRE alpha 2-2 mRNA,... 38 2.9 U04817, HSU04817 Human protein kinase PITSLRE alpha 2-3 mRNA....

HUMAN ESTs

AA639190, AA639190 ns04a01.rl NCI_CGAP_Ewl Homo sapiens cDNA ... 519 e-145 AA172199, AA172199 zo96a06.rl Stratagene ovarian cancer (#937... 513 e-144 R23642, R23642 yh35e03.r1 Homo sapiens cDNA clone 131740 5'. 490 e-136 AA902270, AA902270 ok69e04.s1 NCI CGAP GC4 Homo sapiens cDNA ... 450 e-124 AA947303, AA947303 ok20d04.s1 Soares_NSF_F8_9W_OT_PA_P_S1 Hom... 402 e-110 AA588066, AA588066 nk10d08.s1 NCI_CGAP Co2 Homo sapiens cDNA ... 347 1e-93 AA412036, AA412036 zt68d09.s1 Soares testis NHT Homo sapiens ... 347 1e-93 AA480337, AA480337 ne33a03.s1 NCI_CGAP_Co3 Homo sapiens cDNA ... 347 1e-93 AA508745, AA508745 ni23a03.s1 NCI CGAP Co4 Homo sapiens cDNA ... 347 1e-93 AA172083, AA172083 zo96a06.s1 Stratagene ovarian cancer (#937... 315 4e-84 AA811913, AA811913 ob51d06.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 299 2e-79 AA402403, AA402403 zt68d09.rl Soares testis NHT Homo sapiens ... 299 2e-79 AA725458, AA725458 ai16g01.s1 Soares parathyroid tumor NbHPA ... 250 2e-64 R26558, R26558 yh35e02.s1 Homo sapiens cDNA clone 131738 3'. 250 2e-64 W25749, W25749 11b4 Human retina cDNA randomly primed sublibr... 103 3e-20 W27158, W27158 22h9 Human retina cDNA randomly primed sublibr... 66 6e-09 AA737681, AA737681 nw63c04.s1 NCI CGAP GCB1 Homo sapiens cDNA... T65784, T65784 yc11f10.s1 Homo sapiens cDNA clone 80395 3' si... 42 0.090 R52021, R52021 yg84h09.r1 Homo sapiens cDNA clone 40181 5' si... AA569993, AA569993 nm47h04.s1 NCI_CGAP_Br2 Homo sapiens cDNA ... 42 0.090 R50149, R50149 yj61c05.s1 Homo sapiens cDNA clone 153224 3' s... 42 0.090 R87930, R87930 yo47a11.s1 Homo sapiens cDNA clone 181052 3' s... 42 0.090 AA812204, AA812204 ob84f01.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 42 0.090 AA770224, AA770224 ah82e12.s1 Soares testis NHT Homo sapiens ... 42 0.090

D29591, HUMNK752 Human keratinocyte cDNA, clone 752 40 0.36 AA324325, AA324325 EST27219 Cerebellum II Homo sapiens cDNA 5... AA053063, AA053063 zl71c03.r1 Stratagene colon (#937204) Homo... 40 0.36 T35539, T35539 EST86964 Homo sapiens cDNA 5' end similar to N... 40 0.36 AA974278, AA974278 oq14d03.s1 NCI CGAP GC4 Homo sapiens cDNA ... 40 0.36 W26196, W26196 22b5 Human retina cDNA randomly primed sublibr... 40 0.36 H92585, H92585 yt89c03.s1 Homo sapiens cDNA clone 231460 3'. 40 0.36 AA232334, AA232334 zr27b04.r1 Stratagene NT2 neuronal precurs... 40 0.36 N55775, N55775 J2481F Homo sapiens cDNA clone J2481 5'. 40 0.36 R98701, R98701 yr31f08.s1 Homo sapiens cDNA clone 206919 3'. 40 0.36 C14370, C14370 Human fetal brain cDNA 5'-end GEN-050F01 40 0.36 H19156, H19156 yn50c01.rl Homo sapiens cDNA clone 171840 5'. 40 0.36 AA299557, AA299557 EST12080 Uterus tumor I Homo sapiens cDNA ... 40 0.36 W84460, W84460 zd89d12.rl Soares fetal heart NbHH19W Homo sap... 40 0.36 T54194, T54194 ya90a02.r2 Homo sapiens cDNA clone 68906 5'. 40 0.36 AA100203, AA100203 zm16f12.r1 Stratagene pancreas (#937208) H... 38 1.4 AA993061, AA993061 ot92h08.s1 Soares total fetus Nb2HF8 9w Ho... 38 1.4 R53406, R53406 yj70d07.r1 Homo sapiens cDNA clone 154093 5' s... 38 1.4 H99671, H99671 yx35b03.s1 Homo sapiens cDNA clone 263693 3'. 38 1.4 W03410, W03410 za07c09.rl Soares melanocyte 2NbHM Homo sapien... 38 1.4 N35475, N35475 yy24b03.s1 Homo sapiens cDNA clone 272141 3'. 38 1.4 AA630851, AA630851 nt57f04.s1 NCI CGAP Pr3 Homo sapiens cDNA ... N66458, N66458 yz41b08.s1 Homo sapiens cDNA clone 285591 3'. 38 1.4 AA736438, AA736438 zh31b09.s1 Soares pineal gland N3HPG Homo ... 38 1.4 AA911761, AA911761 og19b01.s1 NCI_CGAP_PNS1 Homo sapiens cDNA... AA085513, AA085513 zn43a10.rl Stratagene HeLa cell s3 937216 ... AA678530, AA678530 ah02e05.s1 Gessler Wilms tumor Homo sapjen... AA782011, AA782011 ai75b12.s1 Soares testis NHT Homo sapiens ... 38 1.4 F12352, HSC38H091 H. sapiens partial cDNA sequence; clone c-... 38 1.4 AA861288, AA861288 ak33g01.s1 Soares testis NHT Homo sapiens ... 38 1.4 AA908705, AA908705 ol01b09.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 38 1.4 AA298850, AA298850 EST114450 Thyroid Homo sapiens cDNA 5' end

AA237204, AA237204 mx18d02.r1 Soares mouse NML Mus musculus c... 172 1e-41 AI047347, AI047347 ud65c01.y1 Sugano mouse liver mlia Mus mus... 42 0.032 AA832736, AA832736 vw45g10.r1 Soares mouse mammary gland NbMM... 42 0.032 AA960471, AA960471 vw63a05.s1 Soares mouse mammary gland NMLM... 40 0.13 AA880584, AA880584 vw92e01.r1 Stratagene mouse skin (#937313)... 40 0.13 AA107508, AA107508 mp05e07.r1 Life Tech mouse embryo 8 5dpc 1... 40 0.13 AA116682, AA116682 mn28c06.r1 Beddington mouse embryonic regi... 40 0.13 AA522310, AA522310 vi45b02.r1 Beddington mouse embryonic regi... 40 0.13 AA162231, AA162231 mn44h02.r1 Beddington mouse embryonic regi... 40 0.13

AA414037, AA414037 vc68g03.s1 Knowles Solter mouse 2 cell Mus... 40 0.13 AA596585, AA596585 vm58e12.rl Stratagene mouse Tcell 937311 M... 38 0.51 AA863563, AA863563 vx05a10.r1 Soares 2NbMT Mus musculus cDNA ... AA795177, AA795177 vq94g04.r1 Knowles Solter mouse blastocyst... 38 0.51 AA914764, AA914764 vy92h04.rl Soares mouse mammary gland NbMM... AA590440, AA590440 vm20c04.r1 Knowles Solter mouse blastocyst... 38 0.51 AA563402, AA563402 vl75d08.rl Knowles Solter mouse blastocyst... 38 0.51 AA260352, AA260352 va93c10.r1 Soares mouse 3NME12 5 Mus muscu... 38 0.51 AA444734, AA444734 ve75d10.r1 Soares mouse mammary gland NbMM... 38 0.51 C85885, C85885 Mus musculus fertilized egg cDNA 3'-end seque... AA794590, AA794590 vu78h12.r1 Stratagene mouse skin (#937313)... 38 0.51 AA529643, AA529643 vi38a09.rl Beddington mouse embryonic regi... 38 0.51 AA607084, AA607084 vm84a09.r1 Knowles Solter mouse blastocyst... AA636994, AA636994 vn05g06.r1 Knowles Solter mouse blastocyst... AA675676, AA675676 vr73h08.s1 Knowles Solter mouse 2 cell Mus... 38 0.51 AA163890, AA163890 ms52f09.r1 Life Tech mouse embryo 13 5dpc ... C80539, C80539 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 38 0.51 AA051352, AA051352 mj53a09.r1 Soares mouse embryo NbME13.5 14... 38 0.51 W36885, W36885 mb64f09.r1 Soares mouse p3NMF19.5 Mus musculus... AA930627, AA930627 vy67c05.r1 Stratagene mouse macrophage (#9... 38 0.51 AA244639, AA244639 mx02g12.rl Soares mouse NML Mus musculus c... AA967267, AA967267 vz70e08.rl Soares mouse mammary gland NbMM... AI048938, AI048938 uc84h06.yl Sugano mouse kidney mkia Mus mu... AA162722, AA162722 mn42b07.r1 Beddington mouse embryonic regi... 36 2.0 AA170036, AA170036 ms52d01.r1 Life Tech mouse embryo 13 5dpc ... AA511382, AA511382 vg14b04.r1 Soares mouse NbMH Mus musculus ... AA555634, AA555634 vk49f08.rl Stratagene mouse Tcell 937311 M... 36 2.0 AA212823, AA212823 mw81c07.rl Soares mouse NML Mus musculus c... AA606813, AA606813 vm90h12.rl Knowles Solter mouse blastocyst... 36 2.0 AA591610, AA591610 vk49d08.r1 Stratagene mouse Tcell 937311 M... 36 2.0 AA987039, AA987039 uc74e05.x1 Sugano mouse liver mlia Mus mus... 36 2.0 AA105882, AA105882 ml84h07.rl Stratagene mouse kidney (#93731... AA451370, AA451370 vf84h02.r1 Soares mouse mammary gland NbMM... AA612185, AA612185 vo03d05.r1 Stratagene mouse skin (#937313)... AA103424, AA103424 mo21e05.rl Life Tech mouse embryo 13 5dpc ... 36 2.0 AA145817, AA145817 mq68a12.r1 Soares 2NbMT Mus musculus cDNA ... 36 2.0 AA272905, AA272905 va39d01.r1 Soares mouse 3NME12 5 Mus muscu... AA237313, AA237313 mx17b11.r1 Soares mouse NML Mus musculus c... AA267119, AA267119 mz74d07.r1 Soares mouse lymph node NbMLN M... 36 2.0 AA106683, AA106683 ml83h06.r1 Stratagene mouse kidney (#93731... 36 2.0 AA125061, AA125061 mq83d10.r1 Stratagene mouse melanoma (#937... 36 2.0 AA655241, AA655241 vq84c07.s1 Knowles Solter mouse 2 cell Mus... AA512835, AA512835 vg13f11.r1 Soares mouse NbMH Mus musculus ... 36 2.0

C70525, C70525 C.elegans cDNA clone yk409g6 : 5' end, single... F15112, SSO4D09 S.scrofa mRNA; expressed sequence tag (5'; c... 42 0.029 AA684640, AA684640 EST104989 Rat PC-12 cells, untreated Rattu... 40 0.11 H32045, H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... AA660422, AA660422 00298 MtRHE Medicago truncatula cDNA 5' 40 0.11 C59696, C59696 C.elegans cDNA clone yk440e1: 3' end, single... 38 0.45 AI008699, AI008699 EST203150 Normalized rat embryo, Bento Soa... AA753263, AA753263 96BS0294 Rice Immature Seed Lambda ZAPII c... 38 0.45 T38461, T38461 EST103957 Saccharomyces cerevisiae cDNA 3' end. 38 0.45 C59257, C59257 C.elegans cDNA clone yk386b12: 3' end, singl... 38 0.45 AA948906, AA948906 LD27590.5prime LD Drosophila melanogaster ... 38 0.45 AI001628, AI001628 EST0210 Tilapia brain cDNA library in pUC1... 38 0.45 H31962, H31962 EST106545 Rat PC-12 cells, untreated Rattus sp... 38 0.45 AA979509, AA979509 LD34118.5prime LD Drosophila melanogaster ... 38 0.45 D41274, RICS3647A Rice cDNA, partial sequence (S3647 1A). 38 0.45 C58362, C58362 C.elegans cDNA clone yk366a8: 3' end, single... 38 0.45 C57756, C57756 C.elegans cDNA clone yk298b9 : 3' end, single... 38 0.45 AA753070, AA753070 97AS2091 Rice Immature Seed Lambda ZAPII c... 38 0.45 H74687, H74687 383 Brassica napus cDNA clone R25R. 38 0.45 C10513, C10513 C.elegans cDNA clone vk147e9: 3' end, single... 38 0.45 C55569, C55569 C.elegans cDNA clone vk191d1: 3' end, single... C94819, C94819 Sus scrofa mRNA; expressed sequence tag (5'; ... C32982, C32982 C.elegans cDNA clone yk338a12: 3' end, singl... AA816691, AA816691 LD03795.5prime LD Drosophila melanogaster ... 36 1.8 AA519844, AA519844 TgESTzz36c03.rl TgME49 invivo Bradyzoite c... AA531839, AA531839 TgESTzz47h05.r1 TgME49 invivo Bradyzoite c... AA660182, AA660182 00022 MtRHE Medicago truncatula cDNA 5' si... D71983, CELK084H2R C.elegans cDNA clone yk84h2: 3' end, sin... 36 1.8 R29905, R29905 12510 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 36 1.8 AA519997, AA519997 TgESTzz36h03.r1 TgME49 invivo Bradyzoite c... 36 1.8 U83048, BTU83048 Bos taurus clone 0429 mRNA sequence 36 1.8 AA440655, AA440655 LD15510.5prime LD Drosophila melanogaster ... AA559374, AA559374 MU002092.NH3 York-Harrop-lung-A Schistosom... C93857, C93857 Dictyostelium discoideum slug cDNA, clone SSL794 36 1.8 AA520901, AA520901 TgESTzz65a05.r1 TgME49 invivo Bradyzoite c... 36 1.8 T46158, T46158 9421 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 AA520866, AA520866 TgESTzz68e05.r1 TgME49 invivo Bradyzoite c... Z17562, ATTS0136 A. thaliana transcribed sequence; clone TAT... 36 1.8 AA520811, AA520811 TgESTzz64d05.rl TgME49 invivo Bradyzoite c... 36 1.8 AA567455, AA567455 HL01288.5prime HL Drosophila melanogaster ... AA519228, AA519228 TgESTzz39h02.s1 TgME49 invivo Bradyzoite c... AA531917, AA531917 TgESTzz48f01.r1 TgME49 invivo Bradyzoite c... AA519829, AA519829 TgESTzz36a02.rl TgME49 invivo Bradyzoite c... 36 1.8 AA520185, AA520185 TgESTzz39d03.s1 TgME49 invivo Bradyzoite c... C37095, C37095 C.elegans cDNA clone yk482c11: 3' end, singl... 36 1.8

T46009, T46009 9272 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 T20458, T20458 2466 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 F14402, ATTS5324 A. thaliana transcribed sequence; clone TAP... 36 1.8 T20404, T20404 2412 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.8 AA274295, AA274295 TgESTzz24c11.s1 TgME49 invivo Bradyzoite c... 36 1.8 AA699152, AA699152 HL07807.5prime HL Drosophila melanogaster ... 36 1.8 AA902065, AA902065 NCM1A12T3 Mycelial Neurospora crassa cDNA ... 36 1.8

SEQ ID NO:558

AF016585, AF016585 Streptomyces caelestis cytochrome P-450 hy... 42 0.092 U50719, MSU50719 Manduca sexta neuroglian mRNA, complete cds 40 0.36 Z97208, SPAC15A10 S.pombe chromosome I cosmid c15A10 40 0.36 AC003063, AC003063 Mus musculus Chromosome 16 BAC Clone b40-o... X66455, MMFGFR2 M.musculus promoter region of fibroblast gro... 40 0.36 D83785, D83785 Human mRNA for KIAA0200 gene, complete cds 40 0.36 AC000398, AC000398 Genomic sequence from Mouse 11, complete s... 38 1.4 AF062345, AF062345 Caulobacter crescentus Sts1 (sts1), S-laye... X12359, RCNIFR12 Rhodobacter capsulatus nifR1 and nifR2 gene 38 1.4 X72382, RCNIFR3 R.capsulatus nifR3 DNA 38 1.4

HUMAN ESTs

R36714, R36714 yh93g06.s1 Homo sapiens cDNA clone 137338 3'. 775 0.0 D61030, HUM149A04B Human fetal brain cDNA 5'-end GEN-149A04. 666 0.0 D60944, HUM141D02B Human fetal brain cDNA 5'-end GEN-141D02. 656 0.0 H03308, H03308 yj47d09.s1 Homo sapiens cDNA clone 151889 3'. 609 e-172 AA435561, AA435561 zt73d09.s1 Soares testis NHT Homo sapiens ... 587 e-166 AA977877, AA977877 oq56d03.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... 571 e-161 AA846787, AA846787 aj41h03.s1 Soares testis NHT Homo sapiens ... 563 e-159 AA972542, AA972542 oo82e01.s1 NCI_CGAP Kid5 Homo sapiens cDNA... 561 e-158 AA954270, AA954270 on72e06.s1 Soares_NFL_T_GBC_S1 Homo sapien... 557 e-157 AA740333, AA740333 ob23c02.s1 NCI CGAP Kid5 Homo sapiens cDNA... 557 e-157 AA999722, AA999722 ov04c06.s1 NCI_CGAP Kid3 Homo sapiens cDNA... 555 e-156 AA970621, AA970621 op40h08.s1 Soares NFL T GBC S1 Homo sapien... 551 e-155 AA932930, AA932930 oo04g11.s1 Soares_NFL_T_GBC_S1 Homo sapien... 541 e-152 AA725406, AA725406 ai13b11.s1 Soares parathyroid tumor NbHPA ... 539 e-152 W74439, W74439 zd75d10.s1 Soares fetal heart NbHH19W Homo sap... 539 e-152 AA868538, AA868538 ak43e08.s1 Soares testis NHT Homo sapiens ... 539 e-152 R79832, R79832 yi89b08.s1 Homo sapiens cDNA clone 146391 3' s... 537 e-151

R63227, R63227 yi07e06.s1 Homo sapiens cDNA clone 138562 3'. AI027967, AI027967 ov84d04.x1 Soares testis NHT Homo sapiens ... 535 e-150 AA776717, AA776717 ah49d07.s1 Soares testis NHT Homo sapiens ... 535 e-150 AI040961, AI040961 ov53d06.x1 Soares testis NHT Homo sapiens ... 533 e-150 AI024835, AI024835 ov35h09.x1 Soares testis NHT Homo sapiens ... 533 e-150 AA740667, AA740667 ob01g12.s1 NCI_CGAP_Kid3 Homo sapiens cDNA... 531 e-149 AA994527, AA994527 ou42h06.s1 Soares NFL T GBC S1 Homo sapien... 531 e-149 AA932728, AA932728 oo31g06.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 529 e-149 AI001978, AI001978 ot39f03.s1 Soares testis NHT Homo sapiens ... 529 e-149 N37092, N37092 yy41g08.s1 Homo sapiens cDNA clone 273854 3'. 529 e-149 N27547, N27547 yy01e05.s1 Homo sapiens cDNA clone 269984 3'. 527 e-148 AA883578, AA883578 al46b08.s1 Soares NFL T GBC S1 Homo sapien... 527 e-148 AA890154, AA890154 al53f07.s1 Soares NFL T GBC S1 Homo sapien... 525 e-147 AA757222, AA757222 ah56f11.s1 Soares testis NHT Homo sapiens ... 525 e-147 AA456074, AA456074 aa17b07.s1 Soares NhHMPu S1 Homo sapiens c... 523 e-147 AA884285, AA884285 am32f04.s1 Soares NFL T GBC S1 Homo sapien... 523 e-147 AA969436, AA969436 op53e12.s1 Soares NFL T GBC S1 Homo sapien... 521 e-146 AA952918, AA952918 on55h11.s1 Soares NFL T GBC S1 Homo sapien... 521 e-146 AA971938, AA971938 op88b01.s1 Soares NFL T GBC S1 Homo sapien... 521 e-146 R25112, R25112 yh36b12.s1 Homo sapiens cDNA clone 131807 3'. 519 e-146 AA865258, AA865258 og87d08.s1 NCI CGAP Kid5 Homo sapiens cDNA... 519 e-146 AA758323, AA758323 ah65e11.s1 Soares testis NHT Homo sapiens ... 519 e-146 AA972041, AA972041 op88e06.s1 Soares NFL T GBC S1 Homo sapien... 519 e-146 R76443, R76443 yi58e11.s1 Homo sapiens cDNA clone 143468 3'. 519 e-146 AA917965, AA917965 om37e04.s1 Soares NFL T GBC S1 Homo sapien... 517 e-145 AA505880, AA505880 ni01a09.s1 NCI_CGAP_Br2 Homo sapiens cDNA ... 517 e-145 AA906270, AA906270 oj98e12.s1 Soares NFL T GBC S1 Homo sapien... 517 e-145 AA758549, AA758549 ah70b04.s1 Soares testis NHT Homo sapiens ... 517 e-145 AA927156, AA927156 om20f05.s1 Soares NFL T GBC S1 Homo sapien... 515 e-144 AA976254, AA976254 oo30f08.s1 NCI CGAP Lu5 Homo sapiens cDNA ... 515 e-144 R23891, R23891 yh28a12.s1 Homo sapiens cDNA clone 131038 3'. 515 e-144 AA938552, AA938552 oo78g11.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... 513 e-144 AA483809, AA483809 ne41c08.s1 NCI CGAP Co3 Homo sapiens cDNA ... 513 e-144 AA962659, AA962659 or31f10.s1 NCI CGAP GC3 Homo sapiens cDNA ... 511 e-143 AA724803, AA724803 ai05f02.s1 Soares parathyroid tumor NbHPA ... 511 e-143 AA410432, AA410432 zv12c09.s1 Soares NhHMPu S1 Homo sapiens c... 511 e-143 AA775373, AA775373 ad19c07.s1 Soares NbHFB Homo sapiens cDNA ... 511 e-143 AA758038, AA758038 ah67h09.s1 Soares testis NHT Homo sapiens ... 509 e-143 AA904368, AA904368 ol15d02.s1 Soares NFL T GBC S1 Homo sapien... 509 e-143 AA861386, AA861386 ak37b11.s1 Soares testis NHT Homo sapiens ... 507 e-142 R31547, R31547 yh72g03.s1 Homo sapiens cDNA clone 135316 3'. 505 e-141 AA843421, AA843421 ak07f11.s1 Soares parathyroid tumor NbHPA ... 504 e-141 H02479, H02479 yi35e10.s1 Homo sapiens cDNA clone 150762 3'. 504 e-141 N29346, N29346 yw85c12.s1 Homo sapiens cDNA clone 259030 3'. 504 e-141 AA815351, AA815351 ai63g05.s1 Soares testis NHT Homo sapiens ... 504 e-141

AA923373, AA923373 ol46e03.s1 Soares_NFL T_GBC_S1 Homo sapien... 502 e-140 H01218, H01218 yi31c08.s1 Homo sapiens cDNA clone 150350 3'. 500 e-140 AA988977, AA988977 or87e11.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 500 e-140 AA628621, AA628621 af40c02.s1 Soares total fetus Nb2HF8 9w Ho... 500 e-140 AA442745, AA442745 zv60a07.s1 Soares testis NHT Homo sapiens ... 498 e-139 AA777492, AA777492 zj02e07.s1 Soares fetal liver spleen 1NFLS... 498 e-139 R73670, R73670 yi55f03.s1 Homo sapiens cDNA clone 143165 3'. 498 e-139 H12460, H12460 yj12d05.s1 Homo sapiens cDNA clone 148521 3'. 498 e-139 AA875917, AA875917 oj15a08.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... 496 e-138 R76230, R76230 yi71g11.s1 Homo sapiens cDNA clone 144740 3'. 494 e-138 AA970616, AA970616 op40h03.s1 Soares_NFL_T_GBC_S1 Homo sapien... 494 e-138 AA912408, AA912408 ol23a05.s1 Soares_NFL T_GBC S1 Homo sapien... 492 e-137 AA910051, AA910051 ol40e08.s1 Soares_NFL T_GBC S1 Homo sapien... 492 e-137 AA815444, AA815444 ai65b11.s1 Soares testis NHT Homo sapiens ... 492 e-137 R76814, R76814 yi62f06.s1 Homo sapiens cDNA clone 143843 3'. 488 e-136 AA954722, AA954722 oo84c12.s1 NCI_CGAP_Kid5 Homo sapiens cDNA... 488 e-136 R65987, R65987 yi23e10.s1 Homo sapiens cDNA clone 140106 3'. 486 e-136 R63480, R63480 yi08e11.s1 Homo sapiens cDNA clone 138668 3'. 486 e-136 AA885425, AA885425 am12h09.s1 Soares NFL T GBC S1 Homo sapien... 486 e-136 AA884231, AA884231 am32a01.s1 Soares NFL T GBC S1 Homo sapien... 484 e-135 AA885048, AA885048 am11a12.s1 Soares NFL T GBC S1 Homo sapien... 482 e-134 AA996162, AA996162 os14f10.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 482 e-134 AA748637, AA748637 ny10a02.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 482 e-134 AI031908, AI031908 ow47e12.x1 Soares_parathyroid_tumor_NbHPA ... 482 e-134 AA884703, AA884703 am18e02.s1 Soares NFL T GBC S1 Homo sapien... 480 e-134 AA928243, AA928243 on87c10.s1 Soares_NFL_T_GBC_S1 Homo sapien... 480 e-134 AI025986, AI025986 ow03a09.s1 Soares_parathyroid tumor NbHPA ... 478 e-133 AA897637, AA897637 oj72g07.s1 Soares_NFL T_GBC S1 Homo sapien... 472 e-131 AA877346, AA877346 01c07.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 472 e-131 AA833569, AA833569 aj46b02.s1 Soares testis NHT Homo sapiens ... 472 e-131 AA832163, AA832163 oc91b02.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 470 e-131 R89052, R89052 ym99e08.s1 Homo sapiens cDNA clone 167078 3'. 470 e-131 N26589, N26589 yx91f03.s1 Homo sapiens cDNA clone 269117 3'. 460 e-128 R73883, R73883 yi56c03.s1 Homo sapiens cDNA clone 143236 3'. 454 e-126 AA579968, AA579968 ng51c03.s1 NCI_CGAP_Co3 Homo sapiens cDNA ... 444 e-123 AA843427, AA843427 ak07g06.s1 Soares parathyroid tumor NbHPA ... 438 e-121 AA705903, AA705903 ah42g12.s1 Soares testis NHT Homo sapiens ... 436 e-121 AA835882, AA835882 oc81d05.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 434 e-120 AA812583, AA812583 aj43b02.s1 Soares testis NHT Homo sapiens ... 432 e-119 AA512970, AA512970 nj16b08.s1 NCI CGAP Pr22 Homo sapiens cDNA... 432 e-119 R26664, R26664 yh35g10.s1 Homo sapiens cDNA clone 131778 3'. AA429715, AA429715 zv60a07.rl Soares testis NHT Homo sapiens ... 414 e-114 H17430, H17430 ym40f09.s1 Homo sapiens cDNA clone 50607 3'. 404 e-111 AA436117, AA436117 zu03d10.r1 Soares testis NHT Homo sapiens ... 402 e-110 AA099077, AA099077 zl77a09.s1 Stratagene colon (#937204) Homo... 400 e-110

R72440, R72440 yj90h02.s1 Homo sapiens cDNA clone 156051 3'. 379 e-103 AA577436, AA577436 nm96h06.s1 NCI_CGAP_Co9 Homo sapiens cDNA ... 351 4e-95 AA516390, AA516390 nf55e03.s1 NCI CGAP Co3 Homo sapiens cDNA ... 347 6e-94 AA534533, AA534533 nf80h06.sl NCI_CGAP_Co3 Homo sapiens cDNA ... 341 3e-92 AA541583, AA541583 ni89f05.s1 NCI_CGAP_Pr21 Homo sapiens cDNA... 311 3e-83 N72191, N72191 yz99f07.s1 Homo sapiens cDNA clone 291205 3'. 303 8e-81 AA905015, AA905015 ok09b08.s1 Soares_NFL T GBC_S1 Homo sapien... 303 8e-81 AA393148, AA393148 zt73d09.rl Soares testis NHT Homo sapiens ... 287 4e-76 AA939048, AA939048 op56h04.s1 Soares_NFL_T_GBC_S1 Homo sapien... 256 2e-66 AA412317, AA412317 zt97c05.rl Soares testis NHT Homo sapiens ... 246 2e-63 R65986, R65986 yi23e10.rl Homo sapiens cDNA clone 140106 5'. 238 4e-61 AA400827, AA400827 zt76c07.s1 Soares testis NHT Homo sapiens ... 232 2e-59 W00472, W00472 yz99f07.rl Homo sapiens cDNA clone 291205 5'. 180 8e-44 AA860558, AA860558 aj81e09.s1 Soares parathyroid tumor NbHPA ... 180 8e-44 AA455577, AA455577 aa17b07.rl Soares NhHMPu S1 Homo sapiens c... 176 1e-42 AA583931, AA583931 nn64e04.s1 NCI_CGAP_Lar1 Homo sapiens cDNA... 172 2e-41 AA907332, AA907332 ol22g11.s1 Soares NFL T GBC S1 Homo sapien... 168 3e-40 R71169, R71169 yi53a12.rl Homo sapiens cDNA clone 142942 5'. 159 3e-37 W79084, W79084 zd75d10.rl Soares fetal heart NbHH19W Homo sap... 155 4e-36 AA295914, AA295914 EST101137 Thymus III Homo sapiens cDNA 5' end 135 4e-30 AA860415, AA860415 aj60d10.s1 Soares testis NHT Homo sapiens ... 100 2e-19 H01351, H01351 yi99a07.rl Homo sapiens cDNA clone 147348 5'. 98 9e-19 AA709286, AA709286 ai21g07.s1 Soares testis NHT Homo sapiens ... 96 3e-18 AA931370, AA931370 oo03d01.sl Soares NFL T GBC S1 Homo sapien... AA501911, AA501911 ng54a08.s1 NCI CGAP Li2 Homo sapiens cDNA ... AA548419, AA548419 nj14g09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA... 92 5e-17 AA588892, AA588892 no23b06.s1 NCI CGAP Pr22 Homo sapiens cDNA... 92 5e-17 AI025228, AI025228 ov40h08.x1 Soares testis NHT Homo sapiens ... 76 3e-12 R73757, R73757 yi55f03.rl Homo sapiens cDNA clone 143165 5'. 74 le-11 R23710, R23710 yh35g10.rl Homo sapiens cDNA clone 131778 5'. 56 3e-06 N40362, N40362 yy01e05.rl Homo sapiens cDNA clone 269984 5'. 50 2e-04 H59895, H59895 yr04c12.r1 Homo sapiens cDNA clone 204310 5'. 48 7e-04 H12509, H12509 yj12d05.rl Homo sapiens cDNA clone 148521 5'. 44 0.011 N20344, N20344 yx38d02.s1 Homo sapiens cDNA clone 264003 3'. 38 0.70 AA614692, AA614692 np52b10.s1 NCI CGAP Br1.1 Homo sapiens cDN... 38 0.70 H30707, H30707 yo78f07.rl Homo sapiens cDNA clone 184069 5'. 36 2.7 H52973, H52973 yq82e04.rl Homo sapiens cDNA clone 202302 5'. 36 2.7 AA218550, AA218550 zq96b02.rl Stratagene NT2 neuronal precurs... 36 2.7 AA312481, AA312481 EST183215 Jurkat T-cells VI Homo sapiens c... 36 2.7 AA632009, AA632009 np74c07.s1 NCI CGAP Br2 Homo sapiens cDNA ... H13363, H13363 yl71b10.r1 Homo sapiens cDNA clone 43343 5'. 36 2.7 AI022018, AI022018 ow64d01.x1 Soares senescent fibroblasts Nb... 36 2.7 AA781996, AA781996 ai75a06.s1 Soares testis NHT Homo sapiens ... 36 2.7 N21623, N21623 yx60a09.s1 Homo sapiens cDNA clone 266104 3'. 36 2.7 AA326194, AA326194 EST29340 Cerebellum II Homo sapiens cDNA 5...

C76071, C76071 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 250 4e-65 AA051612, AA051612 mj52c07.r1 Soares mouse embryo NbME13.5 14... 238 1e-61 AA561635, AA561635 vl01h07.rl Knowles Solter mouse blastocyst... 234 2e-60 AA288419, AA288419 vb14h01.r1 Soares mouse NML Mus musculus c... 220 3e-56 AA212883, AA212883 mw78e10.r1 Soares mouse NML Mus musculus c... 220 3e-56 AA268018, AA268018 vb08e07.r1 Soares mouse NML Mus musculus c... 212 8e-54 AA692427, AA692427 vt59b07.r1 Barstead mouse irradiated colon... 200 3e-50 W18566, W18566 mb98h02.r1 Soares mouse p3NMF19.5 Mus musculus... 192 7e-48 AA543948, AA543948 vj69b08.r1 Knowles Solter mouse blastocyst... 147 4e-34 W41070, W41070 mc39b06.r1 Soares mouse p3NMF19.5 Mus musculus... 123 5e-27 Z31174, MMTEST52 M.musculus expressed sequence tag MTEST52 117 3e-25 AA530723, AA530723 vj32f07.r1 Stratagene mouse diaphragm (#93... 74 5e-12 AA966940, AA966940 ua38c01.rl Soares mouse mammary gland NbMM... AA111079, AA111079 mp50e01.rl Barstead MPLRB1 Mus musculus cD... 44 0.004 AA049187, AA049187 mj51a02.r1 Soares mouse embryo NbME13.5 14... 36 0.99 AA058246, AA058246 mg74e12.rl Soares mouse embryo NbME13.5 14... 36 0.99 AA153730, AA153730 mq60a02.r1 Soares 2NbMT Mus musculus cDNA ... 36 0.99 AA473959, AA473959 vd02b12.s1 Knowles Solter mouse 2 cell Mus... 36 0.99 W47887, W47887 mc83h09.r1 Soares mouse embryo NbME13.5 14.5 M... AA033312, AA033312 mi43g01.rl Soares mouse embryo NbME13.5 14... AA980820, AA980820 ua46a04.rl Soares mouse mammary gland NbMM... Z31139, MMTEST427 M.musculus expressed sequence tag MTEST427 36 0.99 C76637, C76637 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 34 3.9 AI049314, AI049314 uc87b10.y1 Sugano mouse kidney mkia Mus mu... 34 3.9 AA670807, AA670807 vs70b02.r1 Stratagene mouse skin (#937313)... 34 3.9 AA727571, AA727571 vv01h11.r1 Stratagene mouse skin (#937313)... 34 3.9 AA571966, AA571966 vg12f07.r1 Soares mouse NbMH Mus musculus ... 34 3.9 W37059, W37059 mb73f10.r1 Soares mouse p3NMF19.5 Mus musculus... AA760280, AA760280 vv74h11.rl Stratagene mouse skin (#937313)... 34 3.9 AA799036, AA799036 vn40c12.rl Stratagene mouse skin (#937313)... 34 3.9 AA432831, AA432831 vf28g07.r1 Knowles Solter mouse 8 cell Mus... AA562435, AA562435 vk98c01.rl Knowles Solter mouse blastocyst... AA726680, AA726680 vu93g12.r1 Stratagene mouse skin (#937313)... 34 3.9 AA217464, AA217464 mu87d11.r1 Soares mouse lymph node NbMLN M... AA790564, AA790564 vx71e06.r1 Stratagene mouse skin (#937313)... 34 3.9 AA033172, AA033172 mi37f06.rl Soares mouse embryo NbME13.5 14... 34 3.9 AA616204, AA616204 vo96h02.rl Soares mouse mammary gland NbMM... 34 3.9 AA982055, AA982055 ua37h05.rl Soares mouse mammary gland NbMM... 34 3.9 W47850, W47850 mc82h10.rl Soares mouse embryo NbME13.5 14.5 M... 34 3.9 AA537538, AA537538 vk48c12.r1 Soares mouse mammary gland NbMM... 34 3.9 AA636986, AA636986 vn05f04.r1 Knowles Solter mouse blastocyst... 34 3.9

AI043768, AI043768 UI-R-C0-jm-d-11-0-UI.s1 UI-R-C0 Rattus nor... 174 1e-42 AA531635, AA531635 TgESTzz29b08.r1 TgME49 invivo Bradyzoite c... 38 0.22 AA944260, AA944260 EST199759 Normalized rat embryo, Bento Soa... 38 0.22 AI008930, AI008930 EST203381 Normalized rat embryo, Bento Soa... 36 0.87 D15788, RICC1258A Rice cDNA, partial sequence (C1258A). 36 0.87 AA963741, AA963741 UI-R-C0-gt-b-09-0-UI.s1 UI-R-C0 Rattus nor... 36 0.87 AA951235, AA951235 LD31601.3prime LD Drosophila melanogaster ... 34 3.5 C20118, C20118 Rice cDNA, partial sequence (E11542_2A) 34 3.5 AA820317, AA820317 LD23876.5prime LD Drosophila melanogaster ... 34 3.5 AA950448, AA950448 LD30237.3prime LD Drosophila melanogaster ... 34 3.5

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U83883, RNU83883 Rattus norvegicus p105 coactivator mRNA, com... V00722, MMBGL1 Mouse gene for beta-1-globin. X14061, MMBGCXD M.musculus beta-globin complex DNA for y, bh... 40 0.45 U20824, EHVU20824 Equine herpesvirus 2, complete genome 38 1.8 U04106, PFU04106 Pleurotus fossulatus D1822, mating group VI,... 38 1.8 U04101, POU04101 Pleurotus ostreatus D1742, Japan, mating gro... 38 1.8 AC005174, AC005174 Homo sapiens clone UWGC:g1564a012 from 7p1... 38 1.8 M18680, HUMRGAPS Homo sapiens 5S rRNA pseudogene. 38 1.8 AL022121, MTV025 Mycobacterium tuberculosis H37Rv complete g... 38 1.8 AF038379, AF038379 Leishmania amazonensis ribosomal protein S... 38 1.8 Z11528, THIGPMR T.harzianum mRNA for imidazoleglycerolphosphate 38 1.8 U32622, CTU32622 Comamonas testosteroni TsaR (tsaR), toluenes... U04102, POU04102 Pleurotus ostreatus D1743, Japan, mating gro... U04105, PFU04105 Pleurotus fossulatus D1821, mating group VI,... 38 1.8 U04109, PEU04109 Pleurotus eryngii D1832, mating group VI rib... U65606, BSU65606 Basidiomycete from a bamboo (Phyllostachys p... 38 1.8

HUMAN ESTs

R49969, R49969 yj56c07.s1 Homo sapiens cDNA clone 152748 3' s... 523 e-147 AA834501, AA834501 of21c02.s1 NCI_CGAP_Kid6 Homo sapiens cDNA... 381 e-104 W96422, W96422 ze43a05.s1 Soares retina N2b4HR Homo sapiens c... 315 2e-84 R47821, R47821 yj56c07.r1 Homo sapiens cDNA clone 152748 5'. 214 7e-54 AA761660, AA761660 nz24b09.s1 NCI_CGAP_GCB1 Homo sapiens cDNA... 212 3e-53 AA887861, AA887861 nq99b07.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 74 2e-11 AA644044, AA644044 nm20b12.s1 NCI_CGAP_Co10 Homo sapiens cDNA... 72 6e-11

AA115963, AA115963 zm78d11.s1 Stratagene neuroepithelium (#93... AA779271, AA779271 zj43f02.s1 Soares fetal liver spleen 1NFLS... 40 0.22 T65600, T65600 yc76a04.rl Homo sapiens cDNA clone 21496 5'. 38 0.86 AA515882, AA515882 nf67f10.s1 NCI_CGAP Co3 Homo sapiens cDNA ... 38 0.86 AA664812, AA664812 nu69b05.s1 NCI CGAP Alv1 Homo sapiens cDNA... 36 3.4 T83365, T83365 ye03f05.s1 Homo sapiens cDNA clone 116673 3'. 36 3.4 AA009773, AA009773 zi04d04.s1 Soares fetal liver spleen 1NFLS... 36 3.4 AA916894, AA916894 og34g10.s1 NCI CGAP Br7 Homo sapiens cDNA ... 36 3.4 N27865, N27865 vv02g03.s1 Homo sapiens cDNA clone 270100 3'. AA953544, AA953544 om79g06.s1 NCI CGAP Kid3 Homo sapiens cDNA... 36 3.4 AA505576, AA505576 nh93f03.s1 NCI CGAP Br2 Homo sapiens cDNA ... H30276, H30276 yp42f05.s1 Homo sapiens cDNA clone 190113 3'. AA699914, AA699914 zi61f08.s1 Soares fetal liver spleen 1NFLS... 36 3.4 AA595583, AA595583 nk92c04.s1 NCI CGAP Co11 Homo sapiens cDNA... AA351139, AA351139 EST58769 Infant brain Homo sapiens cDNA 5'... 36 3.4 AA810167, AA810167 ob88a03.s1 NCI CGAP GCB1 Homo sapiens cDNA... 36 3.4 H50257, H50257 yo28a07.rl Homo sapiens cDNA clone 179220 5'. W19939, W19939 zb37e09.r1 Soares parathyroid tumor NbHPA Homo... 36 3.4 R19840, R19840 yg30e11.r1 Homo sapiens cDNA clone 33837 5'. 36 3.4 AA514234, AA514234 nf56e10.s1 NCI_CGAP_Co3 Homo sapiens cDNA ... 36 3.4

AA183407, AA183407 ms AA821640, AA821640 vw AA289310, AA289310

AA900756, AA900756 UI-R-E0-di-d-04-0-UI.s1 UI-R-E0 Rattus nor... 46 0.001 T18416, T18416 6c02e07t7 etiolated seedling Zea mays cDNA clo... 40 0.069 AA817427, AA817427 LD22827.5prime LD Drosophila melanogaster ... 36 1.1 AA274351, AA274351 TgESTzz25c09.s1 TgME49 invivo Bradyzoite c... 36 1.1 AA391823, AA391823 LD10747.5prime LD Drosophila melanogaster ... 36 1.1 AA274275, AA274275 TgESTzz24b02.s1 TgME49 invivo Bradyzoite c... 34 4.3 R86490, R86490 RABEST068T Oryctolagus cuniculus cDNA clone pR... 34 4.3 AA965817, AA965817 o5g08a1.r1 Aspergillus nidulans 24hr asexu... 34 4.3

SEQ ID NO:560

X81198, L35746, L49403, U21317, Z35640, AL010273, U09850, AF071771, Z96434,

Z50028, X72735, U13072, Z34294, AB002109, X68401, M92840, D88399, Z36238, AF000262, Z46828,

HUMAN ESTs

AA215808, AA215808 zr98b10.rl NCI_CGAP_GCB1 Homo sapiens cDNA... 1082 0.0 N75131, N75131 yz29g07.rl Soares multiple sclerosis 2NbHMSP H... 989 0.0 AA709149, AA709149 zf98g05.s1 Soares fetal heart NbHH19W Homo... 985 0.0 AA428341, AA428341 zw18f09.s1 Soares ovary tumor NbHOT Homo s... 967 0.0 AA043426, AA043426 zk54h09.rl Soares pregnant uterus NbHPU Ho... 870 0.0 AA878521, AA878521 oj19c01.sl NCI CGAP Kid5 Homo sapiens cDNA... 844 0.0 AA599696, AA599696 ag10h01.s1 Gessler Wilms tumor Homo sapien... 842 0.0 W52304, W52304 zc47c08.rl Soares senescent fibroblasts NbHSF ... 841 0.0 AA043427, AA043427 zk54h09.s1 Soares pregnant uterus NbHPU Ho... 769 0.0 N64314, N64314 yz46a12.s1 Homo sapiens cDNA clone 286078 3'. 763 0.0 N52360, N52360 yz29g07.s1 Soares multiple sclerosis 2NbHMSP H... 753 0.0 AA290863, AA290863 zt19a08.s1 Soares ovary tumor NbHOT Homo s... 747 0.0 AA768023, AA768023 oa60e03.s1 NCI CGAP GCB1 Homo sapiens cDNA... 728 0.0 AA872018, AA872018 oi05f08.s1 NCI CGAP GC4 Homo sapiens cDNA ... 718 0.0 AA164765, AA164765 zp01g09.s1 Stratagene ovarian cancer (#937... 716 0.0 AA814881, AA814881 oa75e02.s1 NCI CGAP GCB1 Homo sapiens cDNA... 708 0.0 R86915, R86915 yq30f07.r1 Homo sapiens cDNA clone 197317 5'. W56703, W56703 zd14e01.rl Soares fetal heart NbHH19W Homo sap... 642 0.0 R84872, R84872 yq27e01.r1 Soares fetal liver spleen 1NFLS Hom... 636 0.0 D79691, HUM307D10B Human aorta cDNA 5'-end GEN-307D10. AA025638, AA025638 ze90d11.sl Soares fetal heart NbHH19W Homo... 626 e-178 AA298883, AA298883 EST114512 Pancreas tumor I Homo sapiens cD... 624 e-177 R86903, R86903 yq30d07.r1 Homo sapiens cDNA clone 197293 5'. AA033584, AA033584 zk21b12.s1 Soares pregnant uterus NbHPU Ho... 618 e-175 AA633335, AA633335 nq58h09.s1 NCI CGAP Co9 Homo sapiens cDNA ... 611 e-173 AA298894, AA298894 EST114513 Pancreas tumor I Homo sapiens cD... 599 e-169 R85806, R85806 yq27e01.s1 Soares fetal liver spleen 1NFLS Hom... 595 e-168 AA872617, AA872617 oi05g07.s1 NCI CGAP GC4 Homo sapiens cDNA ... 591 e-167 H71458, H71458 yu71a06.s1 Homo sapiens cDNA clone 239218 3'. 587 e-166 AA291045, AA291045 zt19a08.rl Soares ovary tumor NbHOT Homo s... 563 e-159 H71587, H71587 yu71a06.rl Homo sapiens cDNA clone 239218 5'. 543 e-153 AA035172, AA035172 zk28g05.s1 Soares pregnant uterus NbHPU Ho... 523 e-147 AA164764, AA164764 zp01g09.rl Stratagene ovarian cancer (#937... 517 e-145 AA297001, AA297001 EST112550 Adipose tissue, white II Homo sa... 502 e-140 AA296816, AA296816 EST112381 Aorta endothelial cells Homo sap... 500 e-139 AA769090, AA769090 oa74e12.s1 NCI CGAP GCB1 Homo sapiens cDNA... 494 e-138 H54447, H54447 yq91f04.s1 Homo sapiens cDNA clone 203167 3'. 438 e-121 H54537, H54537 yq91f04.r1 Homo sapiens cDNA clone 203167 5'. 436 e-120 AI049757, AI049757 an26g03.x1 Gessler Wilms tumor Homo sapien... 430 e-119

<u>naugua nsurar</u>

AA033583, AA033583 zk21b12.rl Soares pregnant uterus NbHPU Ho... 422 e-116 D61748, HUM205G02B Human aorta cDNA 5'-end GEN-205G02. 412 e-113 AA148635, AA148635 zl26d10.rl Soares pregnant uterus NbHPU Ho... 377 e-102 AA148636, AA148636 zl26d10.s1 Soares pregnant uterus NbHPU Ho... 373 e-101 AA025637, AA025637 ze90d11.rl Soares fetal heart NbHH19W Homo... 371 e-101 AA932620, AA932620 oo61h04.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 365 4e-99 AA385594, AA385594 EST99296 Thyroid Homo sapiens cDNA 5' end AA361957, AA361957 EST71295 T-cell lymphoma Homo sapiens cDNA... 289 2e-76 AA383998, AA383998 EST97483 Thyroid Homo sapiens cDNA 5' end ... 274 1e-71 H22175, H22175 yl38a03.rl Homo sapiens cDNA clone 160492 5'. 256 3e-66 R50060, R50060 yj59c10.r1 Homo sapiens cDNA clone 153042 5'. 256 3e-66 AA229414, AA229414 nc47f12.rl NCI CGAP Pr3 Homo sapiens cDNA ... 246 3e-63 D20466, HUMGS01440 Human HL60 3'directed MboI cDNA, HUMGS014... 208 6e-52 AA249061, AA249061 114438.seq.F Human fetal heart, Lambda ZAP... 168 5e-40 R86758, R86758 yq30f07.s1 Homo sapiens cDNA clone 197317 3'. R58025, R58025 F8018 Fetal heart Homo sapiens cDNA clone F801... 101 1e-19 AA371076, AA371076 EST82846 Prostate gland I Homo sapiens cDN... 42 0.081 AA977111, AA977111 oq24c03.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... 40 0.32 AA608923, AA608923 af03b04.s1 Soares testis NHT Homo sapiens ...

gb|AA386999|AA386999 vc81b02.r1 Ko mouse embryo 11 5dpc Mus mus... 668 0.0 gb|AA589082|AA589082 vk24a08.r1 Knowles Solter mouse blastocyst... 658 0.0 gb|AA510881|AA510881 vh59c11.r1 Soares mouse mammary gland NbMM... 617 e-175 gb|AA763574|AA763574 vp07e08.r1 Soares mouse mammary gland NbMM... 615 e-174 gb|AA387423|AA387423 vc84b03.r1 Ko mouse embryo 11 5dpc Mus mus... 549 e-155 gb|AA915333|AA915333 vz28f05.r1 Soares 2NbMT Mus musculus cDNA ... 543 e-153 gb|AA816208|AA816208 vp43c10.rl Barstead mouse irradiated colon... 444 e-123 gb|AA190043|AA190043 mt91h08.r1 Soares mouse lymph node NbMLN M... 424 e-117 gb|AA207393|AA207393 mv89c09.r1 GuayWoodford Beier mouse kidney... 394 e-108 emb|Z31258|MMTEST693 M.musculus expressed sequence tag MTEST693 309 8e-83 gb|AA930143|AA930143 vz52d11.s1 Soares 2NbMT Mus musculus cDNA ... 293 5e-78 gb|AA170612|AA170612 ms92c09.r1 Soares mouse 3NbMS Mus musculus... 287 3e-76 gb|AA762238|AA762238 vw58h02.r1 Soares mouse mammary gland NMLM... 266 1e-69 gb|AA689028|AA689028 vs02c12.r1 Barstead mouse irradiated colon... 264 4e-69 gb|AA959938|AA959938 vw58h02.s1 Soares mouse mammary gland NMLM... 240 6e-62 dbj|D18511|MUSGS01569 Mouse 3'-directed cDNA, MUSGS01569, clon... 172 1e-41 gb|AA474393|AA474393 vd57g07.r1 Knowles Solter mouse blastocyst... 100 1e-19 gb|W97165|W97165 mf90g05.r1 Soares mouse embryo NbME13.5 14.5 M... 74 8e-12 gb|AA512077|AA512077 vj43f05.r1 Stratagene mouse skin (#937313)... 62 3e-08 gb|AA794521|AA794521 vu68e07.r1 Stratagene mouse skin (#937313)... 54 8e-06 gb|AA155454|AA155454 mn38h12.r1 Beddington mouse embryonic regi... 48 5e-04 gb|W91000|W91000 mf83f06.r1 Soares mouse embryo NbME13.5 14.5 M... 40 0.12

gb|AA219917|AA219917 mv62f05.r1 Soares mouse 3NME12 5 Mus muscu... 38 0.45 gb|AA529349|AA529349 vi35f08.r1 Beddington mouse embryonic regi... 36 1.8 gb|AA754855|AA754855 vu51e08.r1 Soares mouse mammary gland NbMM... 36 1.8

gb|AA850379|AA850379 EST193146 Normalized rat ovary, Bento Soar... 569 e-161 gb|W63375|W63375 TgESTzy68g02.rl TgME49 Tachyzoite cDNA Toxopla... 394 e-108 gb|AA946379|AA946379 EST201878 Normalized rat lung, Bento Soare... 353 5e-96 gb|AA964427|AA964427 UI-R-E1-gp-a-08-0-UI.s1 UI-R-E1 Rattus nor... 335 1e-90 gb|AA849599|AA849599 EST192366 Normalized rat muscle, Bento Soa... 307 3e-82 gb|AA849595|AA849595 EST192362 Normalized rat muscle, Bento Soa... 307 3e-82 gb|AA850378|AA850378 EST193145 Normalized rat ovary, Bento Soar... 278 3e-73 gb|AA957389|AA957389 UI-R-E1-fu-b-04-0-UI.s1 UI-R-E1 Rattus nor... 157 6e-37 gb|AI012981|AI012981 EST207432 Normalized rat spleen, Bento Soa... 147 6e-34 dbj|C48357|C48357 C.elegans cDNA clone yk469b2 : 5' end, single... 40 0.10 gb|AA440444|AA440444 LD15290.5prime LD Drosophila melanogaster ... 36 1.6 dbi|C22690|C22690 Rice cDNA, partial sequence (S5274 4A) gb|AA697626|AA697626 HL02895.5prime HL Drosophila melanogaster ... 36 1.6 gb|AA550136|AA550136 1244m3 gmbPfHB3.1, G. Roman Reddy Plasmodi... 36 1.6 gb|T43579|T43579 6842 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 36 1.6 gb|AI030501|AI030501 UI-R-C0-jc-g-02-0-UI.s1 UI-R-C0 Rattus nor... 36 1.6 gb|AA056876|AA056876 SWMFCA987SK Brugia malayi microfilaria cDN... gb|AA440689|AA440689 LD15550.5prime LD Drosophila melanogaster ... 36 1.6

SEQ ID NO:561

emb|Z47552|HSFMO3 H.sapiens mRNA for flavin-containing monooxyg... 44 0.10 gb|U39966|HSFMO3G7 Homo sapiens flavin containing monooxygenase... 44 0.10 emb|AL021026|HS127D3 Homo sapiens DNA sequence from PAC 127D3 o... 44 0.10 gb|U35007|CPU35007 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10 gb|U35008|CPU35008 Carcharhinus plumbeus Ig lambda light chain ... 44 0.10 dbj|D85068|RICT3A Rice transposable element T3 gene and ret... 42 0.40 dbj|D63711|RICT3 Rice transposon T3 DNA, complete sequence 42 0.40 gb|U01657|U01657 Carcharhinus plumbeus Ig lambda-chain gene, co... 42 0.40 emb|Z92540|HS179I15A Human DNA sequence from PAC 179I15, BRCA2 ... 40 1.6 dbj|AB001569|AB001569 Carrot DNA for transposon Tdc1 40 1.6 gb|AE000613|HPAE000613 Helicobacter pylori section 91 of 134 of... 40 1.6 emb|X07985|DMCUT Drosophila cut locus mRNA for homeodomain-cont... 40 1.6 gb|AC005217|AC005217 Homo sapiens chromosome 5, P1 clone 1047D6... 40 1.6

HUMAN ESTs

gb|AA401219|AA401219 zv63a03.r1 Soares total fetus Nb2HF8 9w Ho... 993 0.0 gb|H69371|H69371 yu19h09.rl Homo sapiens cDNA clone 234305 5' s... 44 0.049 gb|N62576|N62576 za13d10.s1 Homo sapiens cDNA clone 292435 3' s... 42 0.19 gb|W77763|W77763 zd69c06.r1 Soares fetal heart NbHH19W Homo sap... 40 0.77 gb|R14832|R14832 yf93g05.r1 Homo sapiens cDNA clone 30203 5'. 40 0.77 gb|T90524|T90524 yd40a04.s1 Homo sapiens cDNA clone 110670 3' s... 38 3.0 gb|R91887|R91887 yq04c09.r1 Homo sapiens cDNA clone 195952 5'. 38 3.0 gb|AA586935|AA586935 nn68h03.s1 NCI_CGAP_Lar1 Homo sapiens cDNA... 38 3.0 gb|T46987|T46987 yb12a07.s1 Homo sapiens cDNA clone 70932 3' co... 38 3.0 gb|AA853975|AA853975 aj51f09.s1 Soares testis NHT Homo sapiens ... 38 3.0 gb|T97059|T97059 ye50e01.r1 Homo sapiens cDNA clone 121176 5'. 38 3.0 gb|AA883119|AA883119 am15h02.s1 Soares NFL T GBC S1 Homo sapien... gb|AA860074|AA860074 ak45b06.s1 Soares testis NHT Homo sapiens ... 38 3.0 gb|AA889618|AA889618 ak28f06.s1 Soares testis NHT Homo sapiens ... 38 3.0

gb|AA230450|AA230450 mv73c06.r1 Soares mouse 3NME12 5 Mus muscu... 38 1.1 gb|AA058041|AA058041 mj58e08.r1 Soares mouse embryo NbME13.5 14... 38 1.1 gb|AA152953|AA152953 mq54a03.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1 gb|W34414|W34414 ma98b07.r1 Soares mouse p3NMF19.5 Mus musculus... 38 1.1 gb|AA465969|AA465969 ve90c06.s1 Knowles Solter mouse 2 cell Mus... 38 1.1 gb|AA261173|AA261173 mz62b11.rl Soares mouse lymph node NbMLN M... 38 1.1 gb|AA238109|AA238109 mw97b05.r1 Soares mouse NML Mus musculus c... dbj|C86549|C86549 Mus musculus fertilized egg cDNA 3'-end seque... 38 1.1 gb|AI048677|AI048677 ub29g09.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.1 dbi|D77921|MUSC1A08 Mouse embryonal carcinoma F9 cell cDNA, C1A08 gb|AA396183|AA396183 vb45e04.r1 Soares mouse lymph node NbMLN M... 38 1.1 gb|AA465898|AA465898 vc62f12.s1 Knowles Solter mouse 2 cell Mus... 36 4.3 gb|AA041869|AA041869 mj05b12.r1 Soares mouse embryo NbME13.5 14... 36 4.3 gb|AA637824|AA637824 vr21f11.rl Barstead mouse myotubes MPLRB5 ... 36 4.3 gb|W82563|W82563 mf05g06.r1 Soares mouse p3NMF19.5 Mus musculus... 36 4.3 gb|AA389972|AA389972 vb30e03.r1 Soares mouse lymph node NbMLN M... 36 4.3 gb|AA396253|AA396253 vb45f08.rl Soares mouse lymph node NbMLN M... 36 4.3 gb|AA920907|AA920907 vy84f04.r1 Stratagene mouse macrophage (#9... 36 4.3 gb|AA517166|AA517166 vh98h05.rl Barstead mouse myotubes MPLRB5 ... 36 4.3 gb|AA433599|AA433599 vf47a05.r1 Soares mouse NbMH Mus musculus ... 36 4.3 gb|AA867252|AA867252 vx25c01.r1 Soares 2NbMT Mus musculus cDNA ... dbj|C85619|C85619 Mus musculus fertilized egg cDNA 3'-end seque... gb|AA260277|AA260277 va93g05.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.3 gb|AA172548|AA172548 mt04g11.r1 Soares mouse 3NbMS Mus musculus... 36 4.3 gb|AA266879|AA266879 mz96a02.r1 Soares mouse lymph node NbMLN M... 36 4.3 gb|AA473019|AA473019 vd43e06.r1 Barstead MPLRB1 Mus musculus cD... 36 4.3

gb|R47549|R47549 SW3ICA119SK Brugia malayi infective larva cDNA... 40 0.24 gb|H32651|H32651 EST107947 Rat PC-12 cells, untreated Rattus sp... 38 0.96 gb|AA955987|AA955987 UI-R-E1-fb-f-06-0-UI.s1 UI-R-E1 Rattus nor... 38 0.96 gblAA819638|AA819638 UI-R-A0-an-f-03-0-UI.s1 UI-R-A0 Rattus nor... 38 0.96 gb|AI010914|AI010914 EST205365 Normalized rat muscle, Bento Soa... 38 0.96 gb|AA893199|AA893199 EST197002 Normalized rat kidney, Bento Soa... gb|AA945176|AA945176 EST200675 Normalized rat liver, Bento Soar... 38 0.96 gb|R95272|R95272 SWOvL3CA167SK Onchocerca volvulus infective la... gb|AA917208|AA917208 ka05f02.s1 Onchocerca volvulus infective l... 36 3.8 dbj|C62023|C62023 C.elegans cDNA clone yk249d5 : 5' end, single... 36 3.8 gb|AI013322|AI013322 EST207997 Normalized rat spleen, Bento Soa... 36 3.8 gb|AI043280|AI043280 TENU0920 T. cruzi epimastigote normalized ... gb|AI009422|AI009422 EST203873 Normalized rat heart, Bento Soar... gb|AI012655|AI012655 EST207106 Normalized rat placenta, Bento S... 36 3.8 dbj|C62878|C62878 C.elegans cDNA clone yk296d4: 5' end, single... 36 3.8 gb|AA915818|AA915818 SWOvL3CA1269SK Onchocerca volvulus infecti... 36 3.8 gb|W00009|W00009 TgESTzy75b07.r1 TgRH Tachyzoite cDNA Toxoplasm... 36 3.8 gb|AA943503|AA943503 EST199002 Normalized rat brain, Bento Soar... 36 3.8 gb|AA956933|AA956933 UI-R-E1-fl-b-08-0-UI.s1 UI-R-E1 Rattus nor... 36 3.8 gblH54977|H54977 HHU16a Sorghum bicolor cv. TX430 Sorghum bicol... 36 3.8

SEQ ID NO:562

gb|AC000112|HSAC000112 Human PAC clone DJ149P21, complete seque... 44 0.082 gb|U50197|CELF25E2 Caenorhabditis elegans cosmid F25E2. 44 0.082 dbj|AB007727|AB007727 Arabidopsis thaliana genomic DNA, chromos... 44 0.082 gb|U02562|BSU02562 Bacillus subtilis N-acetylglucosaminidase (l... 42 0.32 dbj|D45048|BACORFX Bacillus subtilis gene for beta-N-acetylgluc... 42 0.32 emb|Z70683|CEF13B12 Caenorhabditis elegans cosmid F13B12, compl... 40 1.3 emb|AL023828|CEY17G7B Caenorhabditis elegans cosmid Y17G7B, com... 40 1.3 gb|U39740|CELZC64 Caenorhabditis elegans cosmid ZC64. 40 1.3 gb|AF006490|AF006490 Gossypium hirsutum adenine nucleotide tran... 40 1.3 emb|AL010170|PFSC03098 Plasmodium falciparum DNA *** SEQUENCING... 40 1.3 gb|U53701|GHU53701 Gossypium hirsutum alcohol dehydrogenase 2d ... 40 1.3

HUMAN ESTs

gb|AA670455|AA670455 ae62h05.s1 Stratagene lung carcinoma 93721... 852 0.0 gb|AA251062|AA251062 zs07c10.r1 NCI_CGAP_GCB1 Homo sapiens cDNA... 795 0.0

gblAA669916|AA669916 ag42h08.s1 Jia bone marrow stroma Homo sap... 638 0.0 gb|AA300058|AA300058 EST12665 Uterus tumor I Homo sapiens cDNA ... 587 e-165 gb|AA664277|AA664277 ac08c05.s1 Stratagene HeLa cell s3 937216 ... 549 e-154 gb|AA373224|AA373224 EST85230 HSC172 cells I Homo sapiens cDNA ... 529 e-148 gb|AA225705|AA225705 nc10b05.r1 NCI_CGAP_Pr1 Homo sapiens cDNA ... 515 e-144 gb|W27883|W27883 39b10 Human retina cDNA randomly primed sublib... 484 e-134 gb|R24643|R24643 yh36g05.r1 Homo sapiens cDNA clone 131864 5'. 438 e-121 gb|N93137|N93137 zb28h06.s1 Homo sapiens cDNA clone 304955 3'. 432 e-119 gb|AA250933|AA250933 zs07d01.s1 NCI_CGAP GCB1 Homo sapiens cDNA... 426 e-117 gb|AA216370|AA216370 nc10b05.s1 NCI_CGAP_Pr1 Homo sapiens cDNA ... 398 e-109 gb|H26939|H26939 yl64g01.rl Homo sapiens cDNA clone 163056 5'. 394 e-108 gb|H30169|H30169 yo58g09.rl Homo sapiens cDNA clone 182176 5'. 394 e-108 gb|W38854|W38854 zb28h06.rl Soares parathyroid tumor NbHPA Homo... 359 5e-97 gb|AA602297|AA602297 np25a11.s1 NCI CGAP Pr22 Homo sapiens cDNA... 281 1e-73 gb|AA167151|AA167151 zp06e09.rl Stratagene ovarian cancer (#937... 256 6e-66 gb|AA172387|AA172387 zo99d03.s1 Stratagene ovarian cancer (#937... 234 2e-59 gb|AA173748|AA173748 zo99d03.r1 Stratagene ovarian cancer (#937... 224 2e-56 gb|T83979|T83979 yd66a11.s1 Homo sapiens cDNA clone 113180 3'. 220 3e-55 dbi|D61540|HUM415A08B Human fetal brain cDNA 5'-end GEN-415A08. 194 2e-47 gb|N45148|N45148 yv25a05.r1 Homo sapiens cDNA clone 243728 5'. 165 2e-38 gb|AA642960|AA642960 60f07.s1 NCI_CGAP Lym3 Homo sapiens cDNA... 147 4e-33 gb|R90980|R90980 yp93a03.r1 Homo sapiens cDNA clone 194956 5' s... 40 0.62 gb|AA521500|AA521500 aa73h08.s1 NCI CGAP GCB1 Homo sapiens cDNA... 40 0.62 gb|H82921|H82921 yq46h10.s1 Homo sapiens cDNA clone 198883 3' s... 40 0.62 gb|AA294871|AA294871 EST100023 Pancreas tumor I Homo sapiens cD... 38 2.4 dbj|D63191|HUM503F11B Human placenta cDNA 5'-end GEN-503F11. 38 2.4 gb|AA211096|AA211096 zq89g01.s1 Stratagene hNT neuron (#937233)...

gb|AA840137|AA840137 ud01e08.r1 Soares mouse uterus NMPu Mus mu... 383 e-104 gb|AA145994|AA145994 mr13h04.r1 Soares mouse 3NbMS Mus musculus... 345 3e-93 gb|AA146365|AA146365 mr05d05.r1 Soares mouse 3NbMS Mus musculus... 236 2e-60 gb|AA203902|AA203902 mu60f02.r1 Soares mouse lymph node NbMLN M... 236 2e-60 gb|AA204516|AA204516 mu66c10.r1 Soares mouse lymph node NbMLN M... 182 2e-44 gb|AA137343|AA137343 mq80g08.r1 Stratagene mouse melanoma (#937... gb|AA174717|AA174717 ms67a01.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|W34073|W34073 ma85d10.r1 Soares mouse p3NMF19.5 Mus musculus... 48 0.001 gb|AA289493|AA289493 vb36b01.r1 Soares mouse lymph node NbMLN M... 48 0.001 gb|AA177700|AA177700 mt33e12.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|AA146021|AA146021 mr13e03.r1 Soares mouse 3NbMS Mus musculus... 48 0.001 gb|AA155352|AA155352 mn43d09.r1 Beddington mouse embryonic regi... 46 0.004 gb|AA880874|AA880874 vx33b02.r1 Stratagene mouse lung 937302 Mu...

gb|AA590520|AA590520 vi54b08.rl Beddington mouse embryonic regi... gb|AA596629|AA596629 vm56e06.r1 Stratagene mouse Tcell 937311 M... 38 0.88 dbi|D76657|MUS75H09 Mouse embryonal carcinoma F9 cell cDNA, 75H09 38 0.88 gb|AA050336|AA050336 mj12f05.r1 Soares mouse embryo NbME13.5 14... 38 0.88 gb|AA120196|AA120196 mn35a12.rl Beddington mouse embryonic regi... 38 0.88 gb|W85267|W85267 mf42c06.rl Soares mouse embryo NbME13.5 14.5 M... gb|AA239372|AA239372 my38f03.rl Barstead mouse pooled organs MP... gb|AA497891|AA497891 vi73c07.r1 Stratagene mouse testis (#93730... 36 3.5 gb|AA673053|AA673053 vn45e05.r1 Barstead mouse myotubes MPLRB5 ... 36 3.5 emb|Z36324|MM224 M.musculus mRNA (clone 224) for expressed sequ... 36 3.5 gb|AI021128|AI021128 ub01f06.r1 Soares mouse mammary gland NbMM... 36 3.5 gb|AA403424|AA403424 mz56f07.r1 Barstead mouse pooled organs MP... 36 3.5 gb|W66683|W66683 me23g11.r1 Soares mouse embryo NbME13.5 14.5 M... 36 3.5 gb|AA689022|AA689022 vs02c03.r1 Barstead mouse irradiated colon... 36 3.5 gb|AA574590|AA574590 vn63h11.rl Barstead mouse proximal colon M... 36 3.5

dbj|C90696|C90696 Dictyostelium discoideum slug cDNA, clone SSJ634 38 0.78 gb|AA269052|AA269052 MA1MA052.AA3 S. mansoni adult Lambda Zap S... 38 0.78 gb|AA998786|AA998786 UI-R-C0-im-e-11-0-UI.s1 UI-R-C0 Rattus nor... 38 0.78 gb|H33464|H33464 EST109494 Rat PC-12 cells, NGF-treated (9 days... 38 0.78 gb|AA390721|AA390721 LD09459.5prime LD Drosophila melanogaster ... 36 3.1 dbj|C83908|C83908 Dictyostelium discoideum slug cDNA, clone SSA567 36 3.1 gb|AA202425|AA202425 LD02606.5prime LD Drosophila melanogaster ... 36 3.1 gb|AI030951|AI030951 UI-R-C0-jf-d-04-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1 gb|N60251|N60251 TgESTzy11d04.r1 TgRH Tachyzoite cDNA Toxoplasm... 36 3.1 gb|AA246875|AA246875 LD05855.5prime LD Drosophila melanogaster ... 36 3.1 gb|AA997528|AA997528 UI-R-C0-hw-h-11-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1 gb|AA997528|AA997528 UI-R-C0-hw-h-11-0-UI.s1 UI-R-C0 Rattus nor... 36 3.1 gb|AA695197|AA695197 GM02389.5prime GM Drosophila melanogaster ... 36 3.1 gb|AA567339|AA567339 HL01077.5prime HL Drosophila melanogaster ... 36 3.1 gb|AA950648|AA950648 LD30547.5prime LD Drosophila melanogaster ... 36 3.1

SEQ ID NO:563

substantially identical to D86956

SEQ ID NO:564

gb|AC004505|AC004505 Homo sapiens chromosome 20, P1 clone 86C1 ... 176 1e-41 gb|S78798|S78798 1-phosphatidylinositol-4-phosphate 5-kinase is... 115 4e-23 gb|U48696|HSU48696 Human mariner-like element-containing mRNA, ... 115 4e-23 gb|U66300|LEU66300 Lycopersicon esculentum heat shock protein (... 115 4e-23 gb|AF045432|AF045432 Danio rerio stem cell leukemia protein (ta... 111 6e-22 emb|Z97178|BVRNAEF2 Beta vulgaris cDNA for elongation factor 2 107 9e-21 gb|U39066|MMU39066 Murine MAP kinase kinase 6c mRNA, complete cds. 101 6e-19 gb|U37573|XXU37573 Shuttle expression vector pBKCMV. 96 4e-17 gb|AF033097|AF033097 Avena sativa nonphototropic hypocotyl 1 (N... 90 2e-15 gb|AF027174|AF027174 Arabidopsis thaliana cellulose synthase ca... gb|U65376|CFU65376 Canis familiaris rod photoreceptor transduci... 84 1e-13 gb|AF033565|AF033565 Mus musculus cdc2/CDC28-like protein kinas... 82 5e-13 emb|Z49980|HS2AMCP H.sapiens mRNA for ets-like protein (clone 7... 82 5e-13 emb|AJ001103|LLARCAB Lactococcus lactis arcA and arcB genes 80 2e-12 gb|U52868|CFU52868 Canis familiaris retinal cyclic-GMP phosphod... 80 2e-12 gb|G29058|G29058 chicken STS ADL368 76 3e-11 gb|G29060|G29060 chicken STS ADL352 76 3e-11 gb|U34048|HDU34048 Haemophilus ducreyi hemoglobin-binding prote... 76 3e-11 gb|U44386|SLU44386 Solanum lycopersicum heat shock protein (TFH... 68 8e-09 gb|S83098|S83098 ribosomal protein S3 [Ambystoma mexicanum=Mexi... 66 3e-08 gb|U48697|HSU48697 Human mariner-like element-containing mRNA, ... 60 2e-06 gb|AF033096|AF033096 Avena sativa nonphototropic hypocotyl 1 (N... 60 2e-06 emb|X99051|LLATTMSAT L.lagopus ATT microsatellite, locus LLST1 58 8e-06 gb|U41811|HAU41811 Homarus americanus beta-I tubulin mRNA, comp... 46 0.029 emb|X99055|LLCAMSAT1 L.lagopus CA microsatellite, locus LLSD5 44 0.12 emb|X65215|BTMISATN B.taurus microsatellite DNA (624bp) 44 0.12 gb|AE001023|AE001023 Archaeoglobus fulgidus section 84 of 172 o... 42 0.46 emb|X80164|HSPDCM4 H.salinarium phage dcm4 Virus DNA 42 0.46 emb|X87859|MTCMAJ12S C.major mitochondrial gene for 12S ribosom... 42 0.46 emb|X87861|MTCPAL12S C.pallidus mitochondrial gene for 12S ribo... 42 0.46 gb|L13767|STMSEC101A Streptomyus lividans sec101 gene, 5' end p... emb|Y08962|OSTRAMBPR O.sativa mRNA for transmembrane protein >g... gb|S65686|S65686 {multiple cloning sites, vector} [bacteriophag... gb|J02871|HUMCP45IV Human lung cytochrome P450 (IV subfamily) B... 40 1.8 dbj|D10450|HUMRTVE Human genomic DNA, retrovirus-like element 40 1.8 gb|S65683|S65683 {multiple cloning sites, vector} [bacteriophag... gb|L14950|PIGALDRED Sus scrofa aldose reductase mRNA, complete ... gb|S65693|S65693 {multiple cloning sites, vector} [bacteriophag... gb|S65694|S65694 {multiple cloning sites, vector} [bacteriophag... emb|AJ223292|SPAJ3292 Streptococcus pyogenes SOD gene, complete... 40 1.8 gb|U25846|HAU25846 Homarus americanus clone LOB5 farnesoic acid... 40 1.8 emb|X16699|HSP450P2 Human mRNA for cytochrome P-450HP 40 1.8 gb|U37100|HSU37100 Homo sapiens aldose reductase-like peptide m... 40 1.8

HUMAN ESTs

gb|AA305996|AA305996 EST177003 Jurkat T-cells VI Homo sapiens c... 942 0.0 gb|AA975279|AA975279 oq36e08.s1 NCI_CGAP_GC4 Homo sapiens cDNA ... 900 0.0 gb|AA426359|AA426359 zw11b02.rl Soares NhHMPu S1 Homo sapiens c... 868 0.0 gb|AA424296|AA424296 zv90b08.r1 Soares NhHMPu S1 Homo sapiens c... 749 0.0 gb|AA632259|AA632259 np67d04.s1 NCI_CGAP_Br2 Homo sapiens cDNA ... 730 0.0 gb|H80377|H80377 yu59e01.r1 Homo sapiens cDNA clone 230424 5'. 658 0.0 gb|AA515175|AA515175 ng68f10.s1 NCI_CGAP Lip2 Homo sapiens cDNA... 615 e-174 gb|AA351770|AA351770 EST59616 Infant brain Homo sapiens cDNA 5'... 611 e-172 gb|AA426522|AA426522 zw11b02.s1 Soares NhHMPu S1 Homo sapiens c... 587 e-165 gb|AA676220|AA676220 zi22a12.s1 Soares fetal liver spleen 1NFLS... 585 e-165 gb|R35132|R35132 yg60e09.r1 Homo sapiens cDNA clone 36874 5'. 579 e-163 gb|H80280|H80280 yu59e01.s1 Homo sapiens cDNA clone 230424 3'. 579 e-163 gb|H81145|H81145 yu60e01.rl Homo sapiens cDNA clone 230520 5'. 561 e-157 gb|AA311105|AA311105 EST18187 Heart I Homo sapiens cDNA 5' end 533 e-149 gb|AA380530|AA380530 EST93691 Supt cells Homo sapiens cDNA 5' end 527 e-147 gb|H81050|H81050 yu60e01.s1 Homo sapiens cDNA clone 230520 3'. 500 e-139 gb|AA460005|AA460005 zx49g07.s1 Soares testis NHT Homo sapiens ... 482 e-134 gb|AA076450|AA076450 zm91d12.r1 Stratagene ovarian cancer (#937... 466 e-129 gb|N43873|N43873 yy43e09.rl Homo sapiens cDNA clone 274024 5'. 452 e-125 gb|AA076451|AA076451 zm91d12.s1 Stratagene ovarian cancer (#937... 418 e-115 gb|AA907095|AA907095 ol03b12.s1 NCI_CGAP_Lu5 Homo sapiens cDNA ... 414 e-113 gb|W01027|W01027 za56g07.r1 Soares fetal liver spleen 1NFLS Hom... 262 1e-67 gb|AA127183|AA127183 zn29d11.rl Stratagene neuroepithelium NT2R... 222 1e-55 gb|H65491|H65491 yr56a08.s1 Homo sapiens cDNA clone 209270 3'. 222 1e-55 gb|N48543|N48543 yy49d08.r1 Homo sapiens cDNA clone 276879 5'. 210 4e-52 gb|R32579|R32579 yh54h06.r1 Homo sapiens cDNA clone 133595 5'. 194 2e-47 gb|AA247827|AA247827 j0778.seq.F Human fetal heart, Lambda ZAP ... 117 5e-24 N84048, (many others similar, but smaller)

gb|AA589598|AA589598 vl49d08.s1 Stratagene mouse skin (#937313)... 398 e-109 gb|AA647465|AA647465 vq82f02.s1 Knowles Solter mouse 2 cell Mus... 385 e-105 gb|AA510284|AA510284 vh58f02.r1 Soares mouse mammary gland NbMM... 345 4e-93 gb|AA028696|AA028696 mi12e12.r1 Soares mouse p3NMF19.5 Mus musc... 307 9e-82 gb|N28081|N28081 MDB1409R Mouse brain, Stratagene Mus musculus ... 244 1e-62 gb|AA177452|AA177452 mt24c12.r1 Soares mouse 3NbMS Mus musculus... 226 3e-57 gb|N28080|N28080 MDB1409 Mouse brain, Stratagene Mus musculus c... 226 3e-57 dbj|C88310|C88310 Mus musculus fertilized egg cDNA 3'-end seque... 226 3e-57 gb|AA763786|AA763786 vo99g12.r1 Soares mouse mammary gland NbMM... 94 2e-17 gb|AA667535|AA667535 vv18b12.r1 Stratagene mouse heart (#937316... 40 0.31 gb|AA208274|AA208274 mv96a01.r1 GuayWoodford Beier mouse kidney... 38 1.2

gb|AA444814|AA444814 vg50e04.r1 Soares mouse mammary gland NbMM... 38 1.2 gb|AA763341|AA763341 vw53b12.r1 Soares mouse mammary gland NMLM... 38 1.2 gb|AA110827|AA110827 mp57a12.r1 Soares 2NbMT Mus musculus cDNA ... 38 1.2 gb|AA691932|AA691932 vt06b04.r1 Barstead mouse myotubes MPLRB5 ... 38 1,2 gb|W77233|W77233 me61f11.r1 Soares mouse embryo NbME13.5 14.5 M... 38 1.2 gb|AA072872|AA072872 mm80g08.r1 Stratagene mouse embryonic carc... 38 1.2 gb|AA980630|AA980630 ua43f05.r1 Soares mouse mammary gland NbMM... 36 4.9 gb|AA065522|AA065522 ml54d09.r1 Stratagene mouse testis (#93730... 36 4.9 gb|AA982398|AA982398 uh07b08.r1 Soares mouse hypothalamus NMHy ... 36 4.9 gb|W62610|W62610 md58c06.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA286651|AA286651 vb79b02.r1 Soares mouse 3NME12 5 Mus muscu... 36 4.9 gb|AA399772|AA399772 vd70g05.rl Beddington mouse embryonic regi... 36 4.9 gb|AA510475|AA510475 vg32h08.r1 Soares mouse mammary gland NbMM... 36 4.9 gb|AA109064|AA109064 ml63g02.r1 Stratagene mouse testis (#93730... 36 4.9 gb|AA033485|AA033485 mi42c08.r1 Soares mouse embryo NbME13.5 14... 36 4.9 gb|W57221|W57221 md59g10.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA467106|AA467106 vd98b04.r1 Soares mouse NbMH Mus musculus ... 36 4,9 gb|W97470|W97470 mf95a11.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9 gb|AA606917|AA606917 vm91c05.r1 Knowles Solter mouse blastocyst... 36 4.9 dbj|C78330|C78330 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9 gb|AA013753|AA013753 mh26h12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9 gb|AA145240|AA145240 mr12a03.r1 Soares mouse 3NbMS Mus musculus... 36 4.9 gb|AA245533|AA245533 mx03c11.r1 Soares mouse NML Mus musculus c... 36 4.9 gb|AA770893|AA770893 vt13a08.r1 Barstead mouse myotubes MPLRB5 ... 36 4.9 dbj|C79987|C79987 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 36 4.9 gb|AA014027|AA014027 mh24a12.r1 Soares mouse placenta 4NbMP13.5... 36 4.9 dbj|C89051|C89051 Mus musculus early blastocyst cDNA, clone 01B... 36 4.9 gb|AA058308|AA058308 mj59e09.r1 Soares mouse embryo NbME13.5 14... 36 4.9 gb|AA673826|AA673826 vu08h10.r1 Barstead mouse myotubes MPLRB5 ... 36 4.9 gb|AA637080|AA637080 vn07h04.r1 Knowles Solter mouse blastocyst... 36 4.9 gb|W44292|W44292 mc80c07.r1 Soares mouse embryo NbME13.5 14.5 M... 36 4.9

gb|AA955972|AA955972 UI-R-E1-ff-d-10-0-UI.s1 UI-R-E1 Rattus nor... 159 4e-37 gb|AA957275|AA957275 UI-R-E1-fq-f-08-0-UI.s1 UI-R-E1 Rattus nor... 157 2e-36 emb|Z84031|SSZ84031 S.scrofa mRNA; expressed sequence tag (5'; ... 111 9e-23 gb|AF041408|AF041408 Fragaria x ananassa clone FA110b 96 5e-18 gb|AA933116|AA933116 SWBmL3SA048T3 Brugia malayi L3 subtracted ... 58 1e-06 gb|AA933363|AA933363 SWBmL3SA615T3 Brugia malayi L3 subtracted ... 52 7e-05 gb|AA660164|AA660164 00001 MtRHE Medicago truncatula cDNA 5' si... 50 3e-04 gb|N37420|N37420 18647 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018 gb|H35981|H35981 14503 Lambda-PRL2 Arabidopsis thaliana cDNA cl... 44 0.018 gb|AA882627|AA882627 TENS0198 T. cruzi epimastigote normalized ... 44 0.018 gb|AI026481|AI026481 TENU0693 T. cruzi epimastigote normalized ... 42 0.070 gb|AA946369|AA946369 EST201868 Normalized rat lung, Bento Soare... 42 0.070

gb|AI010371|AI010371 EST204822 Normalized rat lung, Bento Soare... 42 0.070 gb|AI010257|AI010257 EST204708 Normalized rat lung, Bento Soare... 42 0.070 dbi|D39318|RICR3325A Rice cDNA, partial sequence (R3325 1A). 40 0.28 gb|U40140|OSU40140 Oryza sativa clone pFDRRC22 mRNA sequence. 40 0.28 gb|AI009132|AI009132 EST203583 Normalized rat embryo, Bento Soa... 40 0.28 dbj|D47291|RICS12574A Rice cDNA, partial sequence (S12574 1A). 40 0.28 dbj|D47316|RICS12613A Rice cDNA, partial sequence (S12613 1A). 40 0.28 gb|T42265|T42265 5528 Lambda-PRL2 Arabidopsis thaliana cDNA clo... 40 0.28 dbj|D47631|RICS13239A Rice cDNA, partial sequence (S13239 1A). 40 0.28 gb|AI013513|AI013513 EST208188 Normalized rat spleen, Bento Soa... 40 0.28 gb|AA751980|AA751980 96AS0896 Rice Immature Seed Lambda ZAPII c... 40 0.28 gb|AA660165|AA660165 00002 MtRHE Medicago truncatula cDNA 5' si... 40 0.28 emb|Z34868|ATTS3597 A. thaliana transcribed sequence; clone FAF... 40 0.28 dbj|D39131|RICR2302A Rice cDNA, partial sequence (R2302 1A). 40 0.28 gb|AA963968|AA963968 UI-R-C0-gs-b-05-0-UI.s1 UI-R-C0 Rattus nor... 40 0.28 gb|AA866346|AA866346 UI-R-A0-bm-a-05-0-UI.s1 UI-R-A0 Rattus nor... 40 0.28 gb|AI044437|AI044437 UI-R-C1-js-e-06-0-UI.s1 UI-R-C1 Rattus nor... 40 0.28 dbj|D41811|RICS4634A Rice cDNA, partial sequence (S4634 1A). 40 0.28 dbj|C19261|C19261 Rice cDNA, partial sequence (E10176 1A) 40 0.28 dbj|D48409|RICS14588A Rice cDNA, partial sequence (S14588 1A). 40 0.28 dbj|C26556|C26556 Rice cDNA, partial sequence (C12586 1A) 40 0.28 dbj|D47831|RICS13548A Rice cDNA, partial sequence (S13548 1A). 40 0.28 dbi|C72152|C72152 Rice cDNA, partial sequence (E1094 3A) 40 0.28 dbj|D46553|RICS11305A Rice cDNA, partial sequence (S11305 2A). 40 0.28 gb|AI028926|AI0289 (and many others of similar score)

SEQ ID NO:565

emb|X68308|OOLPLIP O.ovis mRNA for lipoprotein lipase 40 1.2 gb|AE000660|HUAE000660 Homo sapiens T-cell receptor alpha delta... 40 1.2 emb|AL022333|HS474I12 Human DNA sequence *** SEQUENCING IN PROG... emb|Z12618|CFTRG C.fasciculata gene encoding trypanothione redu... gb|M81651|HUMSEMIIB Human semenogelin II (SEMGII) gene, complet... 38 4.6 gb|M96980|HUMMYT1A Homo sapiens myelin transcription factor 1 (... 38 4.6 gb|U89688|ACU89688 Acanthamoeba castellanii myosin-I binding pr... 38 4.6 gb|AC002497|AC002497 Human Cosmid g1940a142 from 7q31.3, comple... gb|M81652|HUMSMNGLN Homo sapiens semenogelin II mRNA, complete ... 38 4.6 gb|M25665|HUMNCF1A Human neutrophil cytosol factor 1 (NCF-47k) ... 38 4.6 gb|M73325|TRFTRPREDC Crithidia fasciculata trypanothione reduct... 38 4.6 gb|M73324|TRFTRPREDB Crithidia fasciculata trypanothione reduct... 38 4.6 emb|X92589|MMSEMIIGN M.mulatta semenogelin II gene emb|Z47556|HSSG1SG2 H.sapiens genes for semenogelin I and semen... 38 4.6 gb|AC004753|AC004753 Homo sapiens chromosome 16, cosmid clone R... gb|M55067|HUMNADPHO Human 47-kD autosomal chronic granulomatous... 38 4.6 gb|M73323|TRFTRPREDA Crithidia fasciculata trypanothione reduct... 38 4.6

HUMAN ESTs

gb R11942 R11942 yf54c05.r1 Homo sapiens cDNA clone 25950 5'. 656 0.0
gb AA366384 AA366384 EST77326 Pancreas tumor III Homo sapiens c 470 e-130
gb T12566 T12566 CHR90086 Homo sapiens genomic clone P94_24 5' 133 5e-29
gb R37032 R37032 yf54c05.s1 Homo sapiens cDNA clone 25950 3'. 44 0.036
gb AA661650 AA661650 nv02h12.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA261982 AA261982 zs20d03.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA588219 AA588219 no24c11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA250891 AA250891 zs06c06.rl NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA244177 AA244177 nc05a02.r1 NCI_CGAP_Pr1 Homo sapiens cDNA 38 2.2
gb AA715147 AA715147 nv10d05.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA659887 AA659887 nv03a10.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA627890 AA627890 nq70a08.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA603596 AA603596 np27b11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA613738 AA613738 np25h09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA715248 AA715248 nv10h06.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AI038487 AI038487 ow25d12.x1 Soares_parathyroid_tumor_NbHPA 38 2.2
gb AA252786 AA252786 zs26f10.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA287819 AA287819 zs50h04.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA564176 AA564176 nj04c08.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA643870 AA643870 np26h07.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA280371 AA280371 zt05f07.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb R00687 R00687 ye78h08.r1 Homo sapiens cDNA clone 123903 5' s 38 2.2
gb AA587820 AA587820 nj06h05.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA588443 AA588443 no22c11.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA568385 AA568385 nl88f06.s1 NCI_CGAP_Co10 Homo sapiens cDNA 38 2.2
gb AA281831 AA281831 zt06c08.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb AA700438 AA700438 zj74b08.s1 Soares fetal liver spleen 1NFLS 38 2.2
gb AA689530 AA689530 ns66e07.r1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA688300 AA688300 nv14a09.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA687962 AA687962 nv13h04.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA526586 AA526586 ni96f11.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA642589 AA642589 nq73f04.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA541594 AA541594 ni89g07.s1 NCI_CGAP_Pr21 Homo sapiens cDNA 38 2.2
gb AA278713 AA278713 zs76h02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2
gb T58661 T58661 ya94a07.r1 Homo sapiens cDNA clone 69300 5' si 38 2.2
gb AA689473 AA689473 ns66e07.s1 NCI_CGAP_Pr22 Homo sapiens cDNA 38 2.2
gb AA459023 AA459023 aa26a09.r1 NCI_CGAP_GCB1 Homo sapiens cDNA 38 2.2

dbj|C76752|C76752 Mus musculus 3.5-dpc blastocyst cDNA 3'-end s... 60 2e-07 gb|AA123048|AA123048 mn32g01.rl Beddington mouse embryonic regi... 36 3.2 gb|AA616529|AA616529 vo10e01.rl Barstead mouse myotubes MPLRB5 ... 36 3.2 gb|AA254370|AA254370 va13h09.rl Soares mouse lymph node NbMLN M... 36 3.2 gb|AA537288|AA537288 vk46c04.rl Soares mouse mammary gland NbMM... 36 3.2 gb|AA462365|AA462365 vg74c05.rl Soares mouse NbMH Mus musculus ... 36 3.2 gb|AA589462|AA589462 vl47g07.sl Stratagene mouse skin (#937313)... 36 3.2 gb|AA968017|AA968017 uh06h10.rl Soares mouse hypothalamus NMHy ... 36 3.2

dbi|C93868|C93868 Dictyostelium discoideum slug cDNA, clone SSL809 36 2.8 gb|AA531984|AA531984 TgESTzz46b06.r1 TgME49 invivo Bradyzoite c... 36 2.8 gb|N60418|N60418 TgESTzy07a10.r1 TgRH Tachyzoite cDNA Toxoplasm... 36 2.8 gb|H32045|H32045 EST106774 Rat PC-12 cells, untreated Rattus sp... 36 2.8 gb|AA956789|AA956789 UI-R-E1-fr-h-01-0-UI.s1 UI-R-E1 Rattus nor... 36 2.8 gb|H33275|H33275 EST109117 Rat PC-12 cells, NGF-treated (9 days... 36 2.8 gblAA531938|AA531938 TgESTzz45b08.rl TgME49 invivo Bradyzoite c... 36 2.8 dbj|D41507|RICS4044A Rice cDNA, partial sequence (S4044 1A). gb|AA799411|AA799411 EST188908 Normalized rat heart, Bento Soar... 36 2.8 gb|AA519671|AA519671 TgESTzz27c10.r1 TgME49 invivo Bradyzoite c... 36 2.8 dbj|D40678|RICS2786A Rice cDNA, partial sequence (S2786 1A). 36 2.8 gb|AA012430|AA012430 TgESTzz22b12.r1 TgME49cDNA Toxoplasma gond... 36 2.8 dbj|D40551|RICS2612A Rice cDNA, partial sequence (S2612 1A). 36 2.8 gblAI008452|AI008452 EST202903 Normalized rat embryo, Bento Soa... 36 2.8 dbj|D41253|RICS3620A Rice cDNA, partial sequence (S3620 1A). 36 2.8 gb|AA923843|AA923843 UI-R-A1-dr-f-04-0-UI.s1 UI-R-A1 Rattus nor... 36 2.8 gb|AA799410|AA799410 EST188907 Normalized rat heart, Bento Soar... 36 2.8

We claim:

1. A method of diagnosing a disorder characterized by expression of a human cancer associated antigen precursor coded for by a nucleic acid molecule, comprising:

contacting a biological sample isolated from a subject with an agent that specifically binds to the nucleic acid molecule, an expression product thereof, or a fragment of an expression product thereof complexed with an HLA molecule, wherein the nucleic acid molecule is a NA Group 1 nucleic acid molecule, and

determining the interaction between the agent and the nucleic acid molecule or the expression product as a determination of the disorder.

The method of claim 1, wherein the agent is selected from the group consisting of

(a)

a nucleotide acid molecule comprising NA group 1 nucleic acid molecules or a fragment thereof,

(b)

a nucleic acid molecule comprising NA group 3 nucleic acid molecules or

a fragment thereof,

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(c)

a nucleic acid molecule comprising NA group 17 nucleic acid molecules or a fragment thereof,

25 (d)

an antibody that binds to an expression product of NA group 1 nucleic acids,

(e)

an antibody that binds to an expression product of NA group 3 nucleic acids,

(f)

an antibody that binds to an expression product of NA group 17 nucleic acids,

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(g)

and agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 1 nucleic acid,

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(h)

an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 3 nucleic acid, and

(I)

an agent that binds to a complex of an HLA molecule and a fragment of an expression product of a NA group 17 nucleic acid.

- 3. The method of claim 1, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which is specific for a different human cancer associated antigen precursor, and wherein said plurality of agents is at least 2, at least 3, at least 4, at least 6, at least 7, or at least 8, at least 9 or at least 10 such agents.
- 4. The method of claims 1-3, wherein the agent is specific for a human cancer associated antigen precursor that is a breast, a gastric, a lung, a prostate, a renal or a colon cancer associated antigen precursor.
- 5. A method for determining regression, progression or onset of a condition 30 characterized by expression of abnormal levels of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising

monitoring a sample, from a patient who has or is suspected of having the condition, for a parameter selected from the group consisting of

(I)

5 the protein,

(ii)

a peptide derived from the protein,

10 (iii)

an antibody which selectively binds the protein or peptide, and

(iv)

cytolytic T cells specific for a complex of the peptide derived from the protein and an MHC molecule,

as a determination of regression, progression or onset of said condition.

6. The method of claim 5, wherein the sample is a body fluid, a body effusion or a tissue.

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7. The method of claim 5, wherein the step of monitoring comprises contacting the sample with a detectable agent selected from the group consisting of

(a)

an antibody which selectively binds the protein of (I), or the peptide of (ii),

(b)

a protein or peptide which binds the antibody of (iii), and

30 (c)

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12 molecule.

a cell which presents the complex of the peptide and MHC molecule of (iv).

8. The method of claim 7, wherein the antibody, the protein, the peptide or the cell is labeled with a radioactive label or an enzyme.

9. The method of claim 5, comprising assaying the sample for the peptide.

The method of claim 5, wherein the nucleic acid molecule is a NA Group 3 molecule.

11. The method of claim 5, wherein the nucleic acid molecule is a NA Group 11 molecule.

12. The method of claim 5, wherein the nucleic acid molecule is a NA Group

20 13. The method of claim 5, wherein the nucleic acid molecule is a NA Group 13 molecule.

14. The method of claim 5, wherein the nucleic acid molecule is a NA Group 14 molecule.

15. The method of claim 5, wherein the nucleic acid molecule is a NA Group 15 molecule.

The method of claim 5, wherein the nucleic acid molecule is a NA Group 16 molecule.

- 17. The method of claim 5, wherein the protein is a plurality of proteins, the parameter is a plurality of parameters, each of the plurality of parameters being specific for a different of the plurality of proteins.
- A pharmaceutical preparation for a human subject comprising
 an agent which when administered to the subject enriches selectively the
 presence of complexes of an HLA molecule and a human cancer associated antigen, and
 a pharmaceutically acceptable carrier, wherein the human cancer
 associated antigen is a fragment of a human cancer associated antigen precursor encoded by a
 nucleic acid molecule comprises a NA Group 1 molecule.
 - 19. The pharmaceutical preparation of claim 18, wherein the agent comprises a plurality of agents, each of which enriches selectively in the subject complexes of an HLA molecule and a different human cancer associated antigen.
 - 20. The pharmaceutical preparation of claim 19, wherein the plurality is at least two, at least three, at least four or at least 5 different such agents.
- The pharmaceutical preparation of claim 18, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.
 - 22. The pharmaceutical preparation of claim 18, wherein the agent is selected from the group consisting of
 - (1) an isolated polypeptide comprising the human cancer associated antigen, or a functional variant thereof,
 - (2) an isolated nucleic acid operably linked to a promoter for expressing the isolated polypeptide, or functional variant thereof,
 - (3) a host cell expressing the isolated polypeptide, or functional variant thereof, and

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- (4) isolated complexes of the polypeptide, or functional variant thereof, and an HLA molecule.
- The pharmaceutical preparation of claims 18-22, further comprising an adjuvant.
 - 24. The pharmaceutical preparation of claim 18, wherein the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell is nonproliferative.
 - 25. The pharmaceutical preparation of claim 18, wherein the agent is a cell expressing an isolated polypeptide comprising the human cancer associated antigen or a functional variant thereof, and wherein the cell expresses an HLA molecule that binds the polypeptide.
 - 26. The pharmaceutical preparation of claim 18, wherein the agent is at least two, at least three, at least four or at least five different polypeptides, each coding for a different human cancer associated antigen or functional variant thereof.
- 27. The pharmaceutical preparation of claim 18, wherein the agent is a PP Group 2 polypeptide.
 - 28. The pharmaceutical preparation of claim 18, wherein the agent is a PP Group 3 polypeptide or a PP Group 4 polypeptide.
 - 29. The pharmaceutical preparation of claim 25, wherein the cell expresses one or both of the polypeptide and HLA molecule recombinantly.
- The pharmaceutical preparation of claim 25, wherein the cell is nonproliferative.

- 31. A composition comprising
 an isolated agent that binds selectively a PP Group 1 polypeptide.
- 32. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 3 polypeptide.
 - 33. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 11 polypeptide.
- The composition of matter of claim 31, wherein the agent binds selectively a PP Group 12 polypeptide.
 - 35. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 13 polypeptide.
 - 36. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 14 polypeptide.
- 37. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 15 polypeptide.
 - 38. The composition of matter of claim 31, wherein the agent binds selectively a PP Group 16 polypeptide.
- 25 39. The composition of claims 31-38, wherein the agent is a plurality of different agents that bind selectively at least two, at least three, at least four, or at least five different such polypeptides.
 - 40. The composition of claims 31-38, wherein the agent is an antibody.

- 41. The composition of claim 39, wherein the agent is an antibody.
- 42. A composition of matter comprising
 a conjugate of the agent of claims 31-41 and a therapeutic or diagnostic
- 5 agent.
 - 43. The composition of matter of claim 42, wherein the conjugate is of the agent and a therapeutic or diagnostic that is a toxin.
- 10 44. A pharmaceutical composition comprising an isolated nucleic acid molecule selected from the group consisting of:

(1)

NA Group 1 molecules, and

15 (2)

NA Group 2 molecules, and a pharmaceutically acceptable carrier.

- 45. The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises a NA Group 3 or NA Group 4 molecule.
- The pharmaceutical composition of claim 44, wherein the isolated nucleic acid molecule comprises at least two isolated nucleic acid molecules coding for two different polypeptides, each polypeptide comprising a different human cancer associated antigen.
- 25 47. The pharmaceutical composition of claims 44-46 further comprising an expression vector with a promoter operably linked to the isolated nucleic acid molecule.
 - 48. The pharmaceutical composition of claims 44-46 further comprising a host cell recombinantly expressing the isolated nucleic acid molecule.

49.	A pharmaceutical composition comprising
	an isolated polypeptide comprising a PP Group 1 or a PP Group 2
polypeptide, and	
	a pharmaceutically acceptable carrier.

- 50. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises a PP Group 3 or a PP Group 4 polypeptide.
- 10 51. The pharmaceutical composition of claim 49, wherein the isolated polypeptide comprises at least two different polypeptides, each comprising a different human cancer associated antigen.
- 52. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 11 polypeptides or HLA binding fragments thereof.
 - 53. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP
 Group 12 polypeptides or HLA binding fragments thereof.

- 54. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 13 polypeptides or HLA binding fragments thereof.
- 55. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 14 polypeptides or HLA binding fragments thereof.
 - The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 15 polypeptides or HLA binding fragments thereof.

- 57. The pharmaceutical composition of claim 49, wherein the isolated polypeptides are PP Group 16 polypeptides or HLA binding fragments thereof.
- 58. The pharmaceutical composition of claims 49-57, further comprising an adjuvant.
 - 59. An isolated nucleic acid molecule comprising a NA Group 3 molecule.
 - 60. An isolated nucleic acid molecule comprising a NA Group 4 molecule.
- The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 11 molecule or a fragment thereof.
- The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 12 molecule or a fragment thereof.
 - 63. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 13 molecule or a fragment thereof.
- The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 14 molecule or a fragment thereof.
 - 65. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 15 molecule or a fragment thereof.
 - 66. The isolated nucleic acid molecule of claims 59-60, wherein the molecule is a Group 16 molecule or a fragment thereof.
 - 67. An isolated nucleic acid molecule selected from the group consisting of

(a)

a fragment of a nucleic acid selected from the group of nucleic acid consisting of SEQ ID NOs presenting nucleic acid sequences among SEQ ID NOs. 1-816, of sufficient length to represent a sequence unique within the human genome, and identifying a nucleic acid encoding a human cancer associated antigen precursor,

(b)

complements of (a),

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provided that the fragment includes a sequence of contiguous nucleotides which is not identical to any sequence selected from the sequence group consisting of

(1) sequences having the GenBank accession numbers of Table 1

(correct?),

- (2) complements of (1), and
- (3) fragments of (1) and (2).

68. The isolated nucleic acid molecule of claim 67, wherein the sequence of contiguous nucleotides is selected from the group consisting of:

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(1)at least two contiguous nucleotides nonidentical to the sequence group,(2)

) 1 --- 4 41---- - - - - - 4*------

at least three contiguous nucleotides nonidentical to the sequence group,

(3)

at least four contiguous nucleotides nonidentical to the sequence group,

(4)

at least five contiguous nucleotides nonidentical to the sequence group,

(5)

at least six contiguous nucleotides nonidentical to the sequence group,

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(6)

at least seven contiguous nucleotides nonidentical to the sequence group.

- The isolated nucleic acid molecule of claim 67, wherein the fragment has a size selected from the group consisting of at least: 8 nucleotides, 10 nucleotides, 12 nucleotides, 14 nucleotides, 16 nucleotides, 18 nucleotides, 20, nucleotides, 22 nucleotides, 24 nucleotides, 26 nucleotides, 28 nucleotides, 30 nucleotides, 50 nucleotides, 75 nucleotides, 100 nucleotides, and 200 nucleotides.
- The isolated nucleic acid molecule of claim 67, wherein the molecule encodes a polypeptide which, or a fragment of which, binds a human HLA receptor or a human antibody.
- 71. An expression vector comprising an isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69 or 70 operably linked to a promoter.
 - 72. An expression vector comprising a nucleic acid operably linked to a promoter, wherein the nucleic acid is a NA Group 2 molecule.
- 20 73. An expression vector comprising a NA Group 1 or Group 2 molecule and a nucleic acid encoding an HLA molecule.
 - 74. A host cell transformed or transfected with an expression vector of claims 71, 72, or 73.
 - 75. A host cell transformed or transfected with an expression vector of claim 71 or claim 72 and further comprising a nucleic acid encoding HLA.
- 76. An isolated polypeptide encoded by the isolated nucleic acid molecule of claims 59, 60, 61, 62, 63, 64, 65, or 66.

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- 77. A fragment of the polypeptide of claim 76 which is immunogenic.
- 78. The fragment of claim 77, wherein the fragment, or a portion of the fragment, binds HLA or a human antibody.
- 79. An isolated fragment of a human cancer associated antigen precursor which, or portion of which, binds HLA or a human antibody, wherein the precursor is encoded by a nucleic acid molecule that is a NA Group 1 molecule.
- 10 80. The fragment of claim 79, wherein the fragment is part of a complex with HLA.
 - 81. The fragment of claim 79, wherein the fragment is between 8 and 12 amino acids in length.
 - An isolated polypeptide comprising a fragment of the polypeptide of claim 76 of sufficient length to represent a sequence unique within the human genome and identifying a polypeptide that is a human cancer associated antigen precursor.
- 20 83. A kit for detecting the presence of the expression of a human cancer associated antigen precursor comprising a pair of isolated nucleic acid molecules each of which consists essentially

of a molecule selected from the group consisting of

- 25 (a) a 12-32 nucleotide contiguous segment of the nucleotide sequence of any of the NA Group 1 molecules and
 - (b) complements of ("a"), wherein the contiguous segments are nonoverlapping.

- The kit of claim 83, wherein the pair of isolated nucleic acid molecules is constructed and arranged to selectively amplify an isolated nucleic acid molecule that is a NA Group 3 molecule. 85.
- A method for treating a subject with a disorder characterized by 5 expression of a human cancer associated antigen precursor, comprising administering to the subject an amount of an agent, which enriches

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selectively in the subject the presence of complexes of an HLA molecule and a human cancer associated antigen, effective to ameliorate the disorder, wherein the human cancer associated antigen is a fragment of a human cancer associated antigen precursor encoded by a nucleic acid molecule selected from the group consisting of

- (a) a nucleic acid molecule comprising NA group 1 nucleic acid molecules,
- (b) a nucleic acid molecule comprising NA group 3 nucleic acid molecules,
- (c) a nucleic acid molecule comprising NA group 17 nucleic acid molecules.
- 86. The method of claim 85, wherein the disorder is characterized by expression of a plurality of human cancer associated antigen precursors and wherein the agent is a plurality of agents, each of which enriches selectively in the subject the presence of complexes of an HLA molecule and a different human cancer associated antigen.
- 87. The method of claim 86, wherein the plurality is at least 2, at least 3, at least 4, or at least 5 such agents.

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- 88. The method of claims 85-87, wherein the agent is an isolated polypeptide selected from the group consisting of PP Group 1, PP Group 2, PP Group 3, PP Group 4, PP Group 5, PP Group 6, PP Group 7, PP Group 8, PP Group 9, PP Group 10, PP Group 11, PP Group 12, PP Group 13, PP Group 14, PP Group 15, PP Group 16 and PP Group 17 polypeptides.
- 89. The method of claims 85-88, wherein the disorder is cancer.
- 90. A method for treating a subject having a condition characterized by

 10 expression of a human cancer associated antigen precursor in cells of the subject, comprising:
 - (I) removing an immunoreactive cell containing sample from the subject,

15 (ii)

contacting the immunoreactive cell containing sample to the host cell under conditions favoring production of cytolytic T cells against a human cancer associated antigen which is a fragment of the precursor,

20 (iii)

introducing the cytolytic T cells to the subject in an amount effective to lyse cells which express the human cancer associated antigen, wherein the host cell is transformed or transfected with an expression vector comprising an isolated nucleic acid molecule operably linked to a promoter, the isolated nucleic acid molecule being selected from the group of nucleic acid molecules consisting of NA Group 1, NA Group 2, NA Group 3, NA Group 4, NA Group 5, NA Group 6, NA Group 7, NA Group 8, NA Group 9, NA Group 10, NA Group 11, NA Group 12, NA Group 13, NA Group 14, NA Group 15, NA Group 16, and NA Group 17.

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- 91. The method of claim 90, wherein the host cell recombinantly expresses an HLA molecule which binds the human cancer associated antigen.
- 92. The method of claim 90, wherein the host cell endogenously expresses an HLA molecule which binds the human cancer associated antigen.
 - 93. A method for treating a subject having a condition characterized by expression of a human cancer associated antigen precursor in cells of the subject, comprising:

identifying a nucleic acid molecule expressed by the cells associated with said condition, wherein said nucleic acid molecule is a NA Group 1 molecule

transfecting a host cell with a nucleic acid selected from the group consisting of

(ii)

(a) the nucleic acid molecule identified,

(b)

a fragment of the nucleic acid identified which includes a segment coding for a human cancer associated antigen,

(c) deletions, substitutions or additions to (a) or (b), and

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(d)

degenerates of (a), (b), or (c);

(iii)

culturing said transfected host cells to express the transfected nucleic acid molecule, and;

(iv)

introducing an amount of said host cells or an extract thereof to the subject effective to increase an immune response against the cells of the subject associated with the condition.

94. The method of claim 93, further comprising:

(a)

identifying an MHC molecule which presents a portion of an expression product of the nucleic acid molecule,

- wherein the host cell expresses the same MHC molecule as identified in (a) and wherein the host cell presents an MHC binding portion of the expression product of the nucleic acid molecule.
- 95. The method of claim 93, wherein the immune response comprises a B-cell response or a T cell response.
 - 96. The method of claim 95, wherein the response is a T-cell response which comprises generation of cytolytic T-cells specific for the host cells presenting the portion of the expression product of the nucleic acid molecule or cells of the subject expressing the human cancer associated antigen.

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- 97. The method of claim 93, wherein the nucleic acid molecule is a NA Group 3 molecule.
- 98. The method of claims 93 or 94, further comprising treating the host cells to render them non-proliferative.
 - 99. A method for treating or diagnosing or monitoring a subject having a condition characterized by expression of an abnormal amount of a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule, comprising
 - administering to the subject an antibody which specifically binds to the protein or a peptide derived therefrom, the antibody being coupled to a therapeutically useful agent, in an amount effective to treat the condition.
 - The method of claim 99, wherein the antibody is a monoclonal antibody.
 - 101. The method of claim 100, wherein the monoclonal antibody is a chimeric antibody or a humanized antibody.
- 102. A method for treating a condition characterized by expression in a subject of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject a pharmaceutical composition of any one of claims 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 47, and 58 in an amount effective to prevent, delay the onset of, or inhibit the condition in the subject.

- 103. The method of claim 102, wherein the condition is cancer.
- The method of claims 102-103, further comprising first identifying that the subject expresses in a tissue abnormal amounts of the protein.

- 105. A method for treating a subject having a condition characterized by expression of abnormal amounts of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising
- (I) identifying cells from the subject which express abnormal amounts of the protein;
 - (ii) isolating a sample of the cells;
 - (iii) cultivating the cells, and
 - (iv) introducing the cells to the subject in an amount effective to provoke an immune response against the cells.

106. The method of claim 105, wherein the cells express a protein selected from the group

consisting of a PP Group 11 protein, a PP Group 12 protein, a PP Group 13 protein, PP Group 14 protein, a PP Group 15 protein and a PP Group 16 protein.

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- 107. The method of claim 105, further comprising rendering the cells non-proliferative, prior to introducing them to the subject.
- 108. A method for treating a pathological cell condition characterized by
 20 aberrant expression of a protein encoded by a nucleic acid molecule that is a NA Group 1 nucleic acid molecule, comprising

administering to a subject in need thereof an effective amount of an agent which inhibits the expression or activity of the protein.

- The method of claim 108, wherein the agent is an inhibiting antibody which selectively binds to the protein and wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.
- The method of claim 108, wherein the agent is an antisense nucleic acid molecule which selectively binds to the nucleic acid molecule which encodes the protein.

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- 111. The method of claim 108, wherein the nucleic acid molecule is a NA Group 3 nucleic acid molecule.
- 112. A composition of matter useful in stimulating an immune response to a plurality of a protein encoded by nucleic acid molecules that are NA Group 1 molecules, comprising

a plurality of peptides derived from the amino acid sequences of the proteins, wherein the peptides bind to one or more MHC molecules presented on the surface of the cells which express an abnormal amount of the protein.

113. The composition of matter of claim 112, wherein at least a portion of the plurality of peptides bind to MHC molecules and elicit a cytolytic response thereto.

The composition of matter of claim 113, further comprising an adjuvant.

115. The composition of matter of claim 114, wherein said adjuvant is a saponin, GM-CSF, or an interleukin.

116. An isolated antibody which selectively binds to a complex of:

(i)

a peptide derived from a protein encoded by a nucleic acid molecule that is a NA Group 1 molecule and

25 (ii)

and an MHC molecule to which binds the peptide to form the complex, wherein the isolated antibody does not bind to (I) or (ii) alone.

The antibody of claim 116, wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

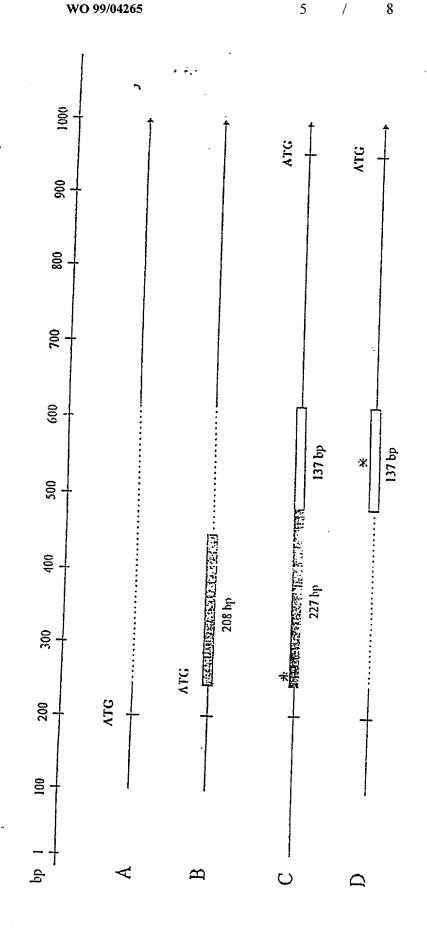
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7.	CCCTIANGAGECATGCTCANAAGAGACACTCTCGTGGCAGAGATTCGCTTCGC	300
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134	GACTATAGGGGTGGAGATCTICTATAGAGTAGGTAGGTAGGTAGTGACTCCATATAAACTACAGGGGAGGGGGGGG	009
167	GENCICATE GACTICAGGGCGCCCCCATTAGALTITAGAGGCCCCCATTGATTTTAGAGATTTTAGAGATTTTTAGAGAGATTTTTAGAGAGATTTTTAGAGAGATTTTTAGAGAGATTTTTAGAGATTTTAGAGAGATTTTAGAGAGATTTTAGAGAGATTTTAG	100
201	S D 1. D F R A R E Q S R S D F R N R D V S D I. D F R D K D G T O V	000
234	GACTY PACAGGC CGAUGAT CAGGTACTACTA GACTY TANGALACACTOR CANTACAGATAT CACAGGTACACACCATCTAGACTICATC OF HG RG S G T T D L H F H D R E S D F R S H H R S R Y D	900
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101	ACHAGATAGAGAACATTGTGGTATGAGAACAGAACAAAAANIXCAGAGAGGAGGAGATAGAAJAGAAGAGGTTKGTTKGGTTTKGGAAGAAAAAAAAAA	1100
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6.3	ANGATANGTCR.CAGCTTTCT.GGACGTGANGAGATCNGATGCTKKATCTGTTTAAAGAAGAAGAKKKKTGTKKACTTTCTTKKGUSGKAAGAGAGA Q D R S Q L S G R K R Q S S D A G L F K K E G G L D F T G R D A G L T K K E G G L D F T G R D A G L C R C A G C L D F T G C R D A G C C C C C C C C C C C C C C C C C C	1300
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Transcript Variant B

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Figure 36.

227bp excn:

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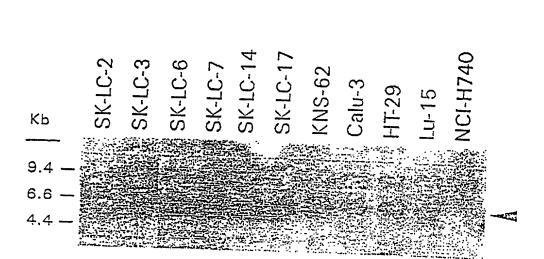


Figure 4

Figures

LVD5499.1 US

Priority

Attorney Docket No. L0461/7078

DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

CANCER ASSOCIATED NUCLEIC ACIDS AND POLYPEPTIDES

the specification of which is attached hereto unless the following is checked:

[X] was filed on July 15, 1998, as PCT application no. PCT/US98/14679, now U.S. application no. 09/462,929, bearing attorney docket no. L0461/7078, and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or section 365(a) of any PCT International application designating at least one country other than the United States listed below and have also identified below any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed:

Prior Foreign PCT International Application(s) and any priority claims under 35 U.S.C. §§119 and 365(a),(b):

			Claimed
9721697.2 (Number)	Great Britain (Country- if PCT, so indicate)	11 October 1997 (DD/MM/YY Filed)	[X] [] YES NO
(Number)	(Country- if PCT, so indicate)	(DD/MM/YY Filed)	[] [] YES NO
(Number)	(Country- if PCT, so indicate)	(DD/MM/YY Filed)	[] [] YES NO

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

60/061,599	10 October 1997
(Application Number)	(filing date)
60/061,765	10 October 1997
(Application Number)	(filing date)

Page 2 of \$4

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s), or §365(c) of any PCT International application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56, which became available between the filing date of the prior application and the national or PCT International filing date of this application:

	17 July 1997	Pending
(Application No.)	(filing date)	(status-patented, pending, abandoned)
08/948,705	10 October 1997	Pending
(Application No.)	(filing date)	(status-patented, pending, abandoned)
09/102,322	22 June 1998	Pending
(Application No.)	(filing date)	(status-patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with

the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Page 4 of 8 4

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<u> </u>	α	Page 4 of \$ 4
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	\sim	9.15.7000
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	Dolldon Wil	robi, England
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Citizenship:	Ugur Sahin	
Residence:	Turkey	
Post Office Address:	Homburg/Saar, Germany	
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		- ,

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Docket No.: E0461/7078

Page 4 of \$4

Inventor's signature Date Full name of sixth joint inventor: Ivan Gout Citizenship: Ukraine Residence: London, England Post Office Address: 91 Riding House Street, London W1P 8BT, England Inventor's signature Date Full name of seventh joint inventor: Michael O'Hare Citizenship: Great Britain Residence: London, England Post Office Address: 91 Riding House Street, London W1P 8BT, England May 8, 2000 Date Inventor's signature Full name of eighth joint inventor: Yuichi Obata Citizenship: Japan Residence: Nagoya, Japan Post Office Address: Chikusa-ku, Nagoya 464, Japan Date Inventor's signature Full name of ninth joint inventor: Michael Pfreundschub Citizenship: Germany Residence: Homburg/Saar, Germany Post Office Address: Med. Klinik I, Universitat des Saarlandes, D-66421 Homburg, Germany Inventor's signature Date Full name of tenth joint inventor: Özlem Türeci Citizenship: Germany Residence: Homburg/Saar, Germany Post Office Address: Med. Klinik I, Universitat des Saarlandes, D-66421 Homburg, Germany

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 O'Hare, Michael
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actgtttcaa agcatgtgac agtggttgga gaactgtctc gattggtcag tgaacggaat
                                                                       360
ctgctggagg tttcagaggt tgagcaagaa ctggcctgtc aaaatgacca ttctagtgct
                                                                       420
ctccagaata taaaaaggct tctgcagaac cccaaagtga cagagtttga tgctgccgc
                                                                       480
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                                                                       540
atgatggncc tcaggaataa aggtgtttct gagaagtatc gaaagctcgt gtctgcagtt
                                                                       600
gttgaatatg gtggtaaaac gagtcagagg aagtgacctc ctcagcccca aagatgctgt
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tggctatcac caaacaattc ctcaaaggg
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                                                                       120
agtgagagtt acagetetta aagatggeac egacecagge egggegeggt ggeteaggee
                                                                       180
tgcaatccca gcactttggg aggcggaggc aggtgaatca cgaggtcagg aaatcgagac
                                                                       240
catcctggct aacatggtga aaccccgtct ccactaaaaa tacaaaaaat tagccaggca
                                                                       300
tggtggctgg cacctgtagt cccagctact tgggaggctg agccaggaaa gtggcatgaa
                                                                       360
cccgcgaggc agagcttgca ataagccgag atcgtgccaa tgcactccag cctgggcaac
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agaaggagac actgtctcaa aaa
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acatttctga tgctcttagt gagcgggata aagtaaaatt cactgttcac acaaagattc
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caccagcacc accaagacct gattttgatg cttcaaggga aaaactacag aagcttggtg
                                                                       240
aaggagaagg gtcaatgacg aaggaagaat tcacaaagat gaaacaggaa ctggaagctg
                                                                       300
aatatttggc aatattcaag aagacagttg cgatgcatga agtgttcctg tgtcgtgtgg
                                                                       360
cagcacatcc tattttgaga agagatttaa atttccatgt cttcttggaa tataatcaag
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atttgagtgt gcgaggaaaa aa
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      <400> 39
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cagtgtggtt ctgtctaacc aaagggcatt ggcctcaaac cctgcatttg gtttagqqqc
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taacagaget ceteagataa tetteacaca catgtaactg etggagatet tattetatta
                                                                       240
tgaataagaa acgagaagtt tttccaaagt gttagtcagg atctqaaqqc tqtcattcaq
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ataacccagc ttttcctttt ggcttttagc ccattcagac tttgccagaq tcaaqccaaq
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gagagaaaga ggatccagga tgtacttgga tgaggaggcc tggcttatct aggaagtcqt
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gtctggggtg cttattgctg ctccatacag ctgtacgtca gccccttggc cttctctqta
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ggttcttggc ancaatgagc agctttcact caagtgacac aaqtaattac tqaqtcctaa
                                                                       600
tttgatagcc accaactgta cctgggtang caaagtcaqa tttttqaqaa nctttttcct
                                                                       660
gatttgaagt tttaattacc ttaatttcct tt
                                                                       692
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                                                                       180
ccaacctcca gcccagagaa gccacaggaa ctcgttacag ctgaggttgc agctccatcc
                                                                       240
acctcatett cagecactte etegeetgag ggteetteae etgeeegace teeteggegt
                                                                       300
cgcaccagtg ctgatgtgga aattaggggt caagggactg gtcggccagg acaaccacca
                                                                       360
ggccccaaag tgcttcgaaa gctgccagga cggctggtaa ctgtggtaga ggaaaaggaa
                                                                       420
ctggtgcggc ggcggcggca gcagcgggga gctgccaanc accctagtgc ctggggtctc
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tgagactagt gccagcccgg gaagcccgtc tgtccgcagc atgtcanggc canaatcctc
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                                                                       600
agnagecett cattgeneg
                                                                       619
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Lys Tyr Leu Met Leu Gly Gln Gln Ala Val Gly Gly Val Pro Ile Gln
            20
Pro Ser Val Arg Thr Gln Met Trp Leu Thr Glu Gln Leu Arg Thr Asn
                            40
Pro Leu Glu Gly Arg Asn Thr Glu Asp Ser Tyr Ser Leu Ala Pro Trp
                                             60
Gln Gln Gln Gln Ile Glu Phe Arg Gln Gly Ser Glu Thr Pro Met Gln
                    70
                                         75
Val Leu Thr Gly Ser Ser Arg Gln Ser Tyr Ser Pro Gly Tyr Gln Asp
                                    90
Phe Ser Lys Trp Glu Ser Met Leu Lys Lys Glu Gly Leu Leu Arg Gln
            100
                                105
                                                     110
Lys Glu Ile Val Asp Arg Gln Lys Gln Ile Thr His Leu Ile Arg Asp
                            120
Asn Glu Leu Pro Ala His Ala Met Leu Gly His Tyr Val Asn Cys Glu
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135

Asp Ser Tyr Val Ala Ser Leu His His 150

<210> 42

<211> 95

<212> PRT

<213> Homo Sapiens

<400> 42

Ile Leu Leu Glu Phe Tyr Leu Trp Gln Ile Gly Arg Tyr Ile Phe Val

His Val Asn Asn His Ile Tyr Ile Lys Leu Tyr Asn Cys Thr Phe Leu 25

Thr Ala Leu Ser Gln Val Ala Leu Ser Phe Pro Ser Ile Asn Gly Leu 40

Ile Phe Val Ser Phe Ala Phe Phe Arg Val Val Asn Ser Tyr Cys Pro Leu Gln Phe Val Gln Phe Leu Arg Cys Leu Leu Leu Lys Arg Met

70 75 Leu Gly Glu Phe Ile Phe His Lys Glu Met Glu His Tyr Leu Lys

<210> 43

<211> 114

<212> PRT

<213> Homo Sapiens

<400> 43

Ser Lys Leu Leu Ser Gly Thr Ala Asp Gly Ala Asp Leu Arg Thr

Val Asp Pro Glu Thr Gln Ala Arg Leu Glu Ala Leu Leu Glu Ala Ala 25

Gly Ile Gly Lys Leu Ser Thr Ala Asp Gly Lys Ala Phe Ala Asp Pro 40

Glu Val Leu Arg Arg Leu Thr Ser Ser Val Ser Cys Ala Leu Asp Glu

Ala Ala Leu Thr Arg Met Arg Ala Glu Ser Thr Ala Asn Ala Gly

Gln Ser Asp Asn Arg Ser Leu Ala Glu Ala Cys Ser Gly Asp Val Ala

Val Arg Lys Leu Leu Ile Glu Gly Arg Ser Val Phe Glu Leu Pro Glu 105

Glu Gly

<210> 44

<211> 132

<212> PRT

<213> Homo Sapiens

<400> 44

Gly Glu Lys Glu Gln Asp Lys Pro Pro Asn Leu Val Leu Lys Asp Lys 10 Val Lys Pro Lys Gln Asp Thr Lys Tyr Asp Leu Ile Leu Asp Glu Gln

25

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Ala Glu Asp Ser Lys Ser Ser His Ser His Thr Ser Lys His Lys
                            40
Lys Thr His His Cys Ser Glu Glu Lys Glu Asp Glu Asp Tyr Met Pro
                        55
Ile Lys Asn Thr Asn Gln Asp Ile Tyr Arg Glu Met Gly Phe Gly His
                    70
Tyr Glu Glu Glu Ser Cys Trp Glu Lys Gln Lys Ser Glu Lys Arg
                85
                                   90
Asp Arg Thr Gln Asn Arg Ser Arg Ser Arg Ser Arg Glu Arg Asp Gly
                                105
His Tyr Ser Asn Ser His Lys Ser Lys Tyr Gln Thr Asp Leu Tyr Glu
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Arg Glu Arg Ser
    130
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      <211> 214
      <212> PRT
      <213> Homo Sapiens
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Lys Ile Arg Lys Glu Met Arg Val Val Asp Arg Gln Ile Arg Asp Ile
Gln Arg Glu Glu Glu Lys Val Lys Arg Ser Val Lys Asp Ala Ala Lys
                            40
Lys Gly Gln Lys Asp Val Cys Ile Val Leu Ala Lys Glu Met Ile Arg
                       55
Ser Arg Lys Ala Val Ser Lys Leu Ala Ser Lys Ala His Met Asn Ser
                    70
                                        75
Val Leu Met Gly Met Lys Asn Gln Leu Ala Val Leu Arg Val Ala Gly
                                    90
Ser Leu Gln Lys Ser Thr Glu Val Met Lys Ala Met Gln Ser Leu Val
           100
                                105
Lys Ile Pro Glu Ile Gln Ala Thr Met Arg Glu Leu Ser Lys Glu Met
                            120
Met Lys Ala Gly Ile Ile Glu Glu Met Leu Glu Asp Thr Phe Glu Ser
                        135
Met Asp Asp Gln Glu Glu Met Glu Glu Glu Ala Glu Met Glu Ile Asp
                    150
                                        155
Arg Ile Leu Phe Glu Ile Thr Ala Gly Ala Leu Gly Lys Ala Pro Ser
                                   170
Lys Val Thr Asp Ala Leu Pro Glu Pro Glu Pro Pro Gly Ala Met Ala
                                185
Ala Ser Glu Asp Glu Glu Glu Glu Glu Leu Glu Ala Met Gln Ser
                            200
                                                205
Arg Leu Ala Thr Arg Ser
    210
      <210> 46
      <211> 248
      <212> PRT
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<213> Homo Sapiens

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> <210> 47 <211> 177 <212> PRT

<213> Homo Sapiens

<400> 47

<210> 48 <211> 102 <212> PRT <213> Homo Sapiens

<400> 48

<210> 49 <211> 179 <212> PRT <213> Homo Sapiens

<400> 49

His Lys Pro Cys Asn Pro Arg Glu Lys Glu Arg Ile Gln Asn Ala Gly 5 Gly Ser Val Met Ile Gln Arg Val Asn Gly Ser Leu Ala Val Ser Arg 25 Ala Leu Gly Asp Tyr Asp Tyr Lys Cys Val Asp Gly Lys Gly Pro Thr 40 Glu Gln Leu Val Ser Pro Glu Pro Glu Val Tyr Glu Ile Leu Arg Ala 55 Glu Glu Asp Glu Phe Ile Ile Leu Ala Cys Asp Gly Ile Trp Asp Val 70 75 Met Ser Asn Glu Glu Leu Cys Glu Tyr Val Lys Ser Arg Leu Glu Val 85 Ser Asp Asp Leu Glu Asn Val Cys Asn Trp Val Val Asp Thr Cys Leu 105 His Lys Gly Ser Arg Asp Asn Met Ser Ile Val Leu Val Cys Phe Ser 120 Asn Ala Pro Lys Val Ser Asp Glu Ala Val Lys Lys Asp Ser Glu Leu 135

Cys Leu Leu

<210> 50 <211> 163 <212> PRT <213> Homo Sapiens

<400> 50

Asp Leu Pro Thr Leu Glu Asp His Gln Lys Gln Ser Gln Gln Leu Lys Asp Ser Glu Leu Lys Ser Thr Glu Leu Gln Glu Lys Val Thr Glu Leu 25 Glu Ser Leu Leu Glu Glu Thr Gln Ala Ile Cys Arg Glu Lys Glu Ile 40 Gln Leu Glu Ser Leu Arg Gln Arg Glu Ala Glu Phe Ser Ser Ala Gly 55 His Ser Leu Gln Asp Lys Gln Ser Val Glu Glu Thr Ser Gly Glu Gly Pro Glu Val Glu Met Glu Ser Trp Gln Lys Arg Tyr Asp Ser Leu Gln Lys Ile Val Glu Lys Gln Gln Gln Lys Met Asp Gln Leu Arg Ser Gln 105 Val Gln Ser Leu Glu Gln Glu Val Ala Glu Glu Gly Thr Ser Gln Ala 115 120 Leu Arg Glu Glu Ala Gln Arg Arg Asp Ser Ala Leu Gln Gln Leu Arg 135 Thr Ala Val Lys Leu Ser Val Asn Gln Asp Leu Ile Glu Lys Asn Leu 150 155

> <210> 51 <211> 164 <212> PRT <213> Homo Sapiens

<400> 51

Thr Leu Gln

 Phe
 Gly
 Asp
 Ser
 Val
 Asp
 Cys
 Ser
 Asp
 Cys
 Trp
 Leu
 Pro
 Val
 Val
 Lys

 Phe
 Ile
 Glu
 Glu
 Glu
 Phe
 Glu
 Glu
 Glu
 Heu
 Arg
 Arg
 Asp
 Glu
 Ser
 Gly
 Leu
 Arg
 Arg
 Glu
 Ser
 Gly
 Leu
 Arg
 Val
 His
 Cys
 Cys
 Leu
 Tyr
 Phe
 Arg
 Phe
 Glu
 Arg
 Arg
 Val
 His
 Cys
 Cys
 Leu
 Tyr
 Phe
 Arg
 Arg
 Arg
 Val
 His
 Phe
 Leu
 Arg
 Arg
 Pro
 Leu
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<210> 52 <211> 600 <212> PRT

<213> Homo Sapiens

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Glu Glu Ala Arg Lys Lys Met Phe Asn Gly Thr Ile Gln Ser Val Pro

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305
                   310
                                       315
Pro Thr Ile Thr Val Leu Pro Ala Gln Leu Ala Pro Thr Lys Met Thr
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                                   330
Gln Pro Ile Leu Gln Thr Ala Leu Pro Cys Gln Ile Leu Gly Gln Thr
                                345
Ser Leu Val Leu Thr Gln Val Thr Ser Gly Ser Thr Thr Val Ser Cys
                           360
                                               365
Ser Pro Ile Thr Leu Ala Val Ala Gly Val Thr Asn His Gly Gln Lys
                       375
Arg Pro Leu Val Thr Pro Gln Ala Ala Pro Glu Pro Lys Arg Pro His
                   390
                                        395
Ile Ala Gln Val Pro Glu Pro Pro Pro Lys Val Ala Asn Pro Pro Leu
                405
                                    410
Thr Pro Ala Ser Asp Arg Lys Lys Thr Lys Glu Gln Ile Ala His Leu
                               425
Lys Ala Ser Phe Leu Gln Ser Gln Phe Pro Asp Asp Ala Glu Val Tyr
                           440
Arg Leu Ile Glu Val Thr Gly Leu Ala Arg Ser Glu Ile Lys Lys Trp
                       455
                                           460
Phe Ser Asp His Arg Tyr Arg Cys Gln Arg Gly Ile Val His Ile Thr
                   470
                                       475
Ser Glu Ser Leu Ala Lys Asp Gln Leu Ala Ile Ala Ala Ser Arg His
                                   490
Gly Arg Thr Tyr His Ala Tyr Pro Asp Phe Ala Pro Gln Lys Phe Lys
                                505
Glu Lys Thr Gln Gly Gln Val Lys Ile Leu Glu Asp Ser Phe Leu Lys
                           520
Ser Ser Phe Pro Thr Gln Ala Glu Leu Asp Arg Leu Arg Val Glu Thr
                       535
Lys Leu Ser Arg Arg Glu Ile Asp Ser Trp Phe Ser Glu Arg Arg Lys
                  550
                                       555
Leu Arg Asp Ser Met Glu Gln Ala Val Leu Asp Ser Met Gly Ser Gly
               565
                                   570
Gln Lys Arg Pro Arg Cys Gly Lys Pro Pro Met Val Leu Cys Leu Asp
                               585
Ser Asn Ser Ser Pro Val Pro Ser
       595
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<210> 53

<211> 163

<212> PRT

<213> Homo Sapiens

<400> 53

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 Trp
 Leu
 Ser
 Trp
 Ala
 Leu
 Asp
 Thr
 Asn
 Glu
 Glu
 Glu
 Arg
 Asp

 Lys
 Gly
 Lys
 Thr
 Val
 Gly
 Arg
 Ala
 Tyr
 Phe
 Glu
 Thr
 Glu
 Lys

 Lys
 His
 Pro
 Thr
 Ile
 Leu
 Asp
 Met
 Asn
 Pro
 Arg
 Thr
 Leu
 Ser
 Lys

 Pro
 Lys
 Ala
 Pro
 Arg
 Pro
 Arg
 Thr
 Leu
 Lys

 Lys
 His
 Pro
 Intraction
 <t

<210> 54

<211> 155

<212> PRT

<213> Homo Sapiens

<400> 54

Glu Arg Trp Pro Glu Glu Gly Thr Ala Asp Leu Ala Gln Ser Gly Leu 10 Glu Gly Gly Thr Thr Arg Ala Ser Val Ser Trp Cys Cys Leu Glu Gly 25 Ser Trp Leu Leu Ser Gly Tyr Leu Thr Phe Leu Lys Thr Cys Ser His Thr Ala Ser Leu Ala Val Ser Ser Ser Ser Cys Arg Ile Arg His Glu Leu Val Pro Asn Ser Ala Arg Gly Lys His Tyr Ser Gln Arg Trp Ala 70 Gln Glu Asp Leu Leu Glu Glu Gln Lys Asp Gly Ala Arg Ala Ala Ala 90 Val Ala Asp Lys Lys Gly Leu Met Gly Pro Leu Thr Glu Leu Asp 1.00 105 Thr Lys Asp Val Asp Ala Leu Leu Lys Lys Ser Glu Ala Gln His Glu 120 125 Gln Pro Glu Asp Gly Cys Pro Phe Gly Ala Leu Thr Gln Arg Leu Leu 135 Gln Ala Leu Val Glu Glu Asn Ile Ile Phe Ser

<210> 55

<211> 112

<212> PRT

<213> Homo Sapiens

150

<400> 55

 Ser
 Glu
 Arg
 Ala
 Leu
 Ala
 Pro
 Arg
 Thr
 Tyr
 Arg
 Met
 Glu
 Thr
 Ala
 Arg
 Arg
 Fro
 Introduction
 Arg
 Fro
 Introduction
 Introductio

Met Gln Ala Leu Met Gln Ile Gln Gln Gly Leu Gln Thr Leu Ala Thr 85 90 95 Glu Ala Pro Gly Leu Ile Pro Ser Phe Thr Pro Gly Val Gly Val Gly 100 105 110

<210> 56

<211> 151

<212> PRT

<213> Homo Sapiens

<400> 56

Lys Phe Gly Met Pro Ile Asp Cys Gly Leu Pro Pro His Ile Asp Phe 1 5 10 15

Gly Asp Cys Thr Lys Leu Lys Asp Asp Gln Gly Tyr Phe Glu Gln Glu 20 25 30

Asp Asp Met Met Glu Val Pro Tyr Val Thr Pro His Pro Pro Tyr His
35 40 45

Leu Gly Ala Val Ala Lys Thr Trp Glu Asn Thr Lys Glu Ser Pro Ala 50 55 60

Thr His Ser Ser Asn Phe Leu Tyr Gly Thr Met Val Ser Tyr Thr Cys 65 70 75 80

Asn Pro Gly Tyr Glu Leu Leu Gly Asn Pro Val Leu Ile Cys Gln Glu
85 90 95

Asp Gly Thr Trp Asn Gly Ser Ala Pro Ser Cys Ile Ser Ile Glu Cys
100 105 110

Asp Leu Pro Thr Ala Pro Glu Asn Gly Phe Leu Arg Phe Thr Glu Thr 115 120 125

Ser Met Gly Ser Ala Val Gln Tyr Ser Cys Lys Pro Gly His Ile Leu 130 135 140

Ala Gly Ser Asp Leu Arg Leu 145 150

<210> 57

<211> 220

<212> PRT

<213> Homo Sapiens

<400> 57

Ala Ala Phe Val Ser Glu Val Thr Ser Phe Pro Val Val Gln Leu His 1 5 10 15

Met Asn Arg Thr Ala Met Arg Ala Ser Gln Lys Asp Phe Glu Asn Ser 20 25 30

Ile Asn Gln Val Lys Leu Leu Lys Lys Asp Pro Gly Asn Glu Val Lys
35 40 45

Leu Lys Leu Tyr Ala Leu Tyr Lys Gln Ala Thr Glu Gly Pro Cys Asn 50 55 60

Met Pro Lys Pro Gly Val Phe Asp Leu Ile Asn Lys Ala Lys Trp Asp 65 70 75 80

Ala Trp Asn Ala Leu Gly Ser Leu Pro Lys Glu Ala Ala Arg Gln Asn 85 90 95

Tyr Val Asp Leu Val Ser Ser Leu Ser Pro Ser Leu Glu Ser Ser Ser 100 105 110

Gln Val Glu Pro Gly Thr Asp Arg Lys Ser Thr Gly Phe Glu Thr Leu
115 120 125

Val Val Thr Ser Glu Asp Gly Ile Thr Lys Ile Met Phe Asn Arg Pro

130 135 140 Lys Lys Lys Asn Ala Ile Asn Thr Glu Met Tyr His Glu Ile Met Arg 150 155 Ala Leu Lys Ala Ala Ser Lys Asp Asp Ser Ile Ile Thr Val Leu Thr 165 170 Gly Asn Gly Asp Tyr Tyr Ser Ser Gly Asn Asp Leu Thr Asn Phe Thr 180 185 Asp Ile Pro Pro Gly Gly Val Glu Lys Ala Lys Asn Asn Ala Val Leu 200 Leu Lys Gly Ile Cys Gly Leu Phe Tyr Arg Ile Ser 210 215 <210> 58 <211> 101 <212> PRT <213> Homo Sapiens <400> 58 Trp Pro Asp Leu Val His Thr Trp Ser Ser Glu Glu Ala Met Gly Ser 10 Cys Cys Ser Cys Pro Asp Lys Asp Thr Val Pro Asp Asn His Arg Asn Lys Phe Lys Val Ile Asn Val Asp Asp Gly Asn Glu Leu Gly Ser 40 Gly Ile Met Glu Leu Thr Asp Thr Glu Leu Ile Leu Tyr Thr Arg Lys 55 Arg Asp Ser Val Lys Trp His Tyr Leu Cys Leu Arg Arg Tyr Gly Tyr 70 Asp Ser Asn Leu Phe Ser Phe Glu Ser Gly Pro Arg Cys Gln Thr Gly 90 Thr Arg Asn Leu Cys 100 <210> 59 <211> 43 <212> PRT <213> Homo Sapiens <400> 59 Ala His Gly Pro Gly Val Glu Pro Thr Ser Arg His Gln Lys Asn Asn 10 Leu Ser Ser Ser His Thr Val Arg Leu Glu Thr Arg Gly Gln Thr Glu 25 Asn Gln Glu Cys Leu Leu Cys Pro His Glu Glu 35 40 <210> 60 <211> 210 <212> PRT <213> Homo Sapiens <400> 60 Leu Asn Gln Trp Thr Tyr Gln Ala Met Val His Glu Leu Leu Gly Ile Asn Asn Asn Arg Ile Asp Leu Ser Arg Val Pro Gly Ile Ser Lys Asp

20 25 Leu Arg Glu Val Val Leu Ser Ala Glu Asn Asp Glu Phe Tyr Ala Asn Asn Met Tyr Leu Asn Phe Ala Glu Ile Gly Ser Asn Ile Lys Asn Leu Met Glu Asp Phe Gln Lys Lys Lys Pro Lys Glu Gln Gln Lys Leu Glu 70 75 Ser Ile Ala Asp Met Lys Ala Phe Val Glu Asn Tyr Pro Gln Phe Lys 90 Lys Met Ser Gly Thr Val Ser Lys His Val Thr Val Val Gly Glu Leu 100 105 Ser Arg Leu Val Ser Glu Arg Asn Leu Leu Glu Val Ser Glu Val Glu 120 Gln Glu Leu Ala Cys Gln Asn Asp His Ser Ser Ala Leu Gln Asn Ile 135 140 Lys Arg Leu Leu Gln Asn Pro Lys Val Thr Glu Phe Asp Ala Ala Arg 150 155 Leu Val Met Leu Tyr Ala Leu His Tyr Glu Arg His Ser Ser Asn Ser 165 170 Leu Pro Gly Leu Met Met Leu Arg Asn Lys Gly Val Ser Glu Lys Tyr 185 Arg Lys Leu Val Ser Ala Val Val Glu Tyr Gly Gly Lys Thr Ser Gln 200 Arg Lys 210 <210> 61 <211> 40 <212> PRT <213> Homo Sapiens <400> 61 Thr Pro Gly Pro Gly Ala Gly Phe Tyr Ala Cys Pro Ala Arg Pro Leu 1.0 Val Ser Gly Ile Tyr Ser Phe Arg Trp Val Arg Gly Leu Ala Asp Gln Glu Arg Asn Trp Gly Leu Ser Gln 35 <210> 62 <211> 238 <212> PRT <213> Homo Sapiens <400> 62 His Glu Ala Arg Leu Lys Arg Ala Ser Ala Pro Thr Phe Asp Asn Asp 10 Tyr Ser Leu Ser Glu Leu Leu Ser Gln Leu Asp Ser Gly Val Ser Gln Ala Val Glu Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Ser Lys Leu Pro Ser Ser Gly Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val 60 Asp Ser Ala Phe Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg

Glu Pro Ser Thr Ser Asp Leu Gly Thr Thr Asp Val Gln Lys Lys Leu Val Asp Ala Ile Val Ser Gly Asp Thr Ser Lys Leu Met Lys Ile 105 Leu Gln Pro Gln Asp Val Asp Leu Ala Leu Asp Ser Gly Ala Ser Leu 120 Leu His Leu Ala Val Glu Ala Gly Gln Glu Cys Ala Lys Trp Leu 135 Leu Leu Asn Asn Ala Asn Pro Asn Leu Ser Asn Arg Arg Gly Ser Thr 150 155 Pro Leu His Met Ala Val Glu Arg Arg Val Arg Gly Val Val Glu Leu 165 1.70 Leu Leu Ala Arg Ile Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr 185 Ala Leu His Phe Ala Asn Gly Gly Val His Thr Ala Ala Val Gly Glu 200 Arg Leu Gly Gln Thr Lys Val Asp Phe Glu Gly Arg Thr Pro Met Gln 215 220 Val Gly Leu Pro Thr Thr Gly Lys Asn Ile Leu Arg Ile Leu 230

<210> 63

<211> 146

<212> PRT

<213> Homo Sapiens

<400> 63

Arg Leu Gly Ala Ala Met Met Glu Gly Leu Asp Asp Gly Pro Asp Phe 5 Leu Ser Glu Glu Asp Arg Gly Leu Lys Ala Ile Asn Val Asp Leu Gln 25 Ser Asp Ala Ala Leu Gln Val Asp Ile Ser Asp Ala Leu Ser Glu Arg 40 Asp Lys Val Lys Phe Thr Val His Thr Lys Ile Pro Pro Ala Pro Pro 55 60 Arg Pro Asp Phe Asp Ala Ser Arg Glu Lys Leu Gln Lys Leu Gly Glu 70 Gly Glu Gly Ser Met Thr Lys Glu Glu Phe Thr Lys Met Lys Gln Glu Leu Glu Ala Glu Tyr Leu Ala Ile Phe Lys Lys Thr Val Ala Met His 105 Glu Val Phe Leu Cys Arg Val Ala Ala His Pro Ile Leu Arg Arg Asp 120 Leu Asn Phe His Val Phe Leu Glu Tyr Asn Gln Asp Leu Ser Val Arg

135

Gly Lys 145

<210> 64

<211> 63 <212> PRT

<213> Homo Sapiens

<400> 64

Glu Arg Gly His Ser Ile Lys Asp Phe Val Ser Phe Ala Arg His Phe

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                 5
                                    10
Ser Pro Asn Pro Arg Ile Val Ser Val Asn Ala Ser Tyr Ser Leu Ser
                                25
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Pro Pro Ser Ala Ala Ser Asp Glu Pro Leu Gln Glu Pro Leu Glu Ala
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Asp Arg Thr Ser Glu Glu Leu Thr Glu Ala Lys Thr Pro Thr Ser Ser
Pro Glu Lys Pro Gln Glu Leu Val Thr Ala Glu Val Ala Ala Pro Ser
                    70
Thr Ser Ser Ser Ala Thr Ser Ser Pro Glu Gly Pro Ser Pro Ala Arg
                85
                                    90
Pro Pro Arg Arg Thr Ser Ala Asp Val Glu Ile Arg Gly Gln Gly
                                105
Thr Gly Arg Pro Gly Gln Pro Pro Gly Pro Lys Val Leu Arg Lys Leu
                            120
                                                125
Pro Gly Arg Leu Val Thr Val Val Glu Glu Lys Glu Leu Val Arg Arg
                        135
                                            140
Arg Arg Gln Gln Arg Gly Ala Ala Ser Thr Leu Val Pro Gly Val Ser
                    150
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Glu Thr Ser Ala Ser Pro Gly Ser Pro Ser Val Arg Ser Met Ser Gly
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Ser Ser Leu Pro Thr Pro Pro
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gctatgcgaa attatttaaa agggtaaggg gatcaaatag tacttatcct tcatgcaaaa
                                                                       240
gttgtacaga agtcatatgg caatcaaaaa atttttttt gccctccccc ttgtgtatat
                                                                       300
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                                                                       360
cacagetete atecatgtge atttattggg ataggaaata gtgaccaaga aatgeageag
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ctaaacttgg aaggaaagaa ctattgcaca gccaaaacat tgtacatatc tgattcagac
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	taccag atacttgcat				720
cagcagtggg gagca	atttta cattcaatto	: ttggatgatg	atggatcaga	aggagaagaa	780
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actggcatgg cacto	cccaag attgataatt	atgaaagttg	ataagcatac	cgcattattg	900
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ggacagaatt tcac	tccaaa tttacgagtg	, tggtttgggg	gggtagaagc	tgaaactatg	1260
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<210> 67

<211> 729

<212> PRT

<213> Homo Sapiens

<400> 67

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225					230					235					240
His	Val	Lys	Val	Leu 245	Asn	Thr	Ser	Leu	Lys 250	Glu	Lys	Phe	Asn	Gly 255	Lys
Lys	Ile	Ile	Ile 260	Ile	Ser	Asp	Tyr	Leu 265	Glu	Tyr	Asp	Ser	Leu 270	Leu	Glu
		275					280					285		Thr	
	290					295					300			Lys	
305					310					315				Val	320
				325					330					Glu 335	
			340					345				_	350	Cys	
		355					360					365	_	Phe	_
	370					375					380			His	
385					390					395			_	Pro	400
				405					410					Ser 415	
			420					425					430	Met	
		435					440					445		Asp	
	450					455					460		_	Glu	_
465					470					475				Glu	480
				485					490					Ser 495	
			500					505					510	Val	
		515					520					525		Leu	
	530					535					540			Met	
545					550					555					Phe 560
				565					570					Ala 575	
			580					585					590		Thr
		595					600					605		Lys	_
	610					615					620			Cys	
GIn 625	Thr	Lys	Gly	Ser	Phe 630	Val	Asn	Gly	Val	Phe 635	Glu	Val	His	Lys	Lys 640
	Val	Arg	Gly	Glu 645		Thr	Tyr	Tyr	Glu 650		Gln	Asp	Asn	Thr 655	Gly
Lys	Met	Glu	Val 660	Val	Val	His	Gly	Arg 665	Leu	Asn	Thr	Ile	Asn 670		Glu

Glu Gly Asp Lys Leu Lys Leu Thr Ser Phe Glu Leu Ala Pro Lys Ser 680 Gly Asn Thr Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val 695 700 Ile Lys Thr Lys Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser 710 715 Met Glu Thr Ser Pro Asp Phe Phe 725

<210> 68 <211> 754 <212> PRT

<213> Homo Sapiens

<400> 68

Met Ala Ser Val Pro Ala Leu Gln Leu Thr Pro Ala Asn Pro Pro Pro 10 Pro Glu Val Ser Asn Pro Lys Lys Pro Gly Arg Val Thr Asn Gln Leu 25 Gln Tyr Leu His Lys Val Val Met Lys Ala Leu Trp Lys His Gln Phe Ala Trp Pro Phe Arg Gln Pro Val Asp Ala Val Lys Leu Gly Leu Pro Asp Tyr His Lys Ile Ile Lys Gln Pro Met Asp Met Gly Thr Ile Lys Arg Arg Leu Glu Asn Asn Tyr Tyr Trp Ala Ala Ser Glu Cys Met Gln 85 90 Asp Phe Asn Thr Met Phe Thr Asn Cys Tyr Ile Tyr Asn Lys Pro Thr 105 Asp Asp Ile Val Leu Met Ala Gln Thr Leu Glu Lys Ile Phe Leu Gln 120 Lys Val Ala Ser Met Pro Gln Glu Glu Glu Glu Leu Val Val Thr Ile 135 140 Pro Lys Asn Ser His Lys Lys Gly Ala Lys Leu Ala Ala Leu Gln Gly 150 155 Ser Val Thr Ser Ala His Gln Val Pro Ala Val Ser Ser Val Ser His 165 170 Thr Ala Leu Tyr Thr Pro Pro Pro Glu Ile Pro Thr Thr Val Leu Asn 185 Ile Pro His Pro Ser Val Ile Ser Ser Pro Leu Leu Lys Ser Leu His 200 205 Ser Ala Gly Pro Pro Leu Leu Ala Val Thr Ala Ala Pro Pro Ala Gln 215 220 Pro Leu Ala Lys Lys Gly Val Lys Arg Lys Ala Asp Thr Thr 230 235 Pro Thr Pro Thr Ala Ile Leu Ala Pro Gly Ser Pro Ala Ser Pro Pro 245 250 Gly Ser Leu Glu Pro Lys Ala Ala Arg Leu Pro Pro Met Arg Arg Glu Ser Gly Arg Pro Ile Lys Pro Pro Arg Lys Asp Leu Pro Asp Ser Gln 280 Gln Gln His Gln Ser Ser Lys Lys Gly Lys Leu Ser Glu Gln Leu Lys 295 300 His Cys Asn Gly Ile Leu Lys Glu Leu Leu Ser Lys Lys His Ala Ala

	Ala			325					330					335	
	qaA		340					345					350		
	Arg	355					360					365			
	Asp 370					375					380				
Asp 385	His	Asp	Val	Val	Ala 390	Met	Ala	Arg	Lys	Leu 395	Gln	Asp	Val	Phe	Glu 400
	Arg			405					410				_	415	
	Val		420					425					430		
	Ser	435					440					445			
	Glu 450					455					460				-
465	Glu				470					475					480
	Ala			485					490					495	
	Pro		500					505					510		_
	Glu	51 5					520					525	-	_	-
	Arg 530					535					540	_	-		
545	Ser				550					555				_	560
	Gly			565					570					575	
	Pro		580					585					590		
	Pro	595					600					605	_		
	Leu 610					615					620				
625					630					635					640
	Glu			645					650					655	
	Ser		660					665					670		
	Val	675					680					685			
	Glu 690					695					700				
705	Pro				710					715					720
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ser	Gly														

<210> 69 <211> 210 <212> PRT <213> Homo Sapiens

<400> 69

Met Asp Asp Glu Glu Glu Thr Tyr Arg Leu Trp Lys Ile Arg Lys Thr Ile Met Gln Leu Cys His Asp Arg Gly Tyr Leu Val Thr Gln Asp Glu Leu Asp Gln Thr Leu Glu Glu Phe Lys Ala Gln Phe Gly Asp Lys Pro 40 Ser Glu Gly Arg Pro Arg Arg Thr Asp Leu Thr Val Leu Val Ala His Asn Asp Asp Pro Thr Asp Gln Met Phe Val Phe Pro Glu Glu Pro 70 Lys Val Gly Ile Lys Thr Ile Lys Val Tyr Cys Gln Arg Met Gln Glu 90 Glu Asn Ile Thr Arg Ala Leu Ile Val Val Gln Gln Gly Met Thr Pro 105 Ser Ala Lys Gln Ser Leu Val Asp Met Ala Pro Lys Tyr Ile Leu Glu 120 125 Gln Phe Leu Gln Gln Glu Leu Leu Ile Asn Ile Thr Glu His Glu Leu 135 140 Val Pro Glu His Val Val Met Thr Lys Glu Glu Val Thr Glu Leu Leu 150 155 Ala Arg Tyr Lys Leu Arg Glu Asn Gln Leu Pro Arg Ile Gln Ala Gly 170 Asp Pro Val Ala Arg Tyr Phe Gly Ile Lys Arg Gly Gln Val Lys 180 185 Ile Ile Arg Pro Ser Glu Thr Ala Gly Arg Tyr Ile Thr Tyr Arg Leu 200

<210> 70

Val Gln 210

<211> 621

<212> PRT

<213> Homo Sapiens

<400> 70

 Met
 Leu
 Leu
 Pro
 Ser
 Ala
 Ala
 Glu
 Gly
 Gly
 Thr
 Ala
 Ile
 Thr

 1

His	Val	Arg	Tyr 100	Thr	Ala	Thr	Gln	Arg 105	Gln	Ile	Lys	Ala	Ala	His	Lys
Ala	Met	Val 115	Leu	Lys	His	His	Pro 120	Asp	Lys	Arg	Lys	Ala 125	Ala	Gly	Glu
	130					135					140			Lys	
145					150					155				Ser	160
				165					170					Lys 175	_
			180					185					190	Arg	_
		195					200					205		Ser	
	210					215					220			Ser	_
225					230					235				Glu	240
				245					250					Arg 255	
			260					265					270	Asp	
		275					280					285		Glu	_
	290					295					300			Arg	
305					310					315				Ala	320
				325					330					Ala 335	
			340					345					350	Lys	
		355					360					365		Ser	_
	370					375					380			Leu	_
385					390					395				Leu	400
				405					410					Ile 415	
			420					425					430	Ala	
		435					440					445		Ser	_
	450					455					460			Ile	_
465					470					475				Val	480
				485					490					Thr 495	
			500					505					510	Pro	
		515					520					525		Lys	
His	Gly	Val	Ala	Ser	Gln	Ala	Asp	Ser	Ala	Ala	Pro	Ser	Glu	Arg	Phe

530 535 540 Glu Gly Pro Cys Ile Asp Ser Thr Pro Trp Thr Thr Glu Glu Gln Lys 550 555 Leu Leu Glu Gln Ala Leu Lys Thr Tyr Pro Val Asn Thr Pro Glu Arg 565 570 Trp Glu Lys Ile Ala Glu Ala Val Pro Gly Arg Thr Lys Lys Asp Cys 580 585 Met Arg Arg Tyr Lys Glu Leu Val Glu Met Val Lys Ala Lys Lys Ala 600 Ala Gln Glu Gln Val Leu Asn Ala Ser Arg Ala Arg Lys 610 615

<210> 71 <211> 267

<212> PRT

<213> Homo Sapiens

<400> 71

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> <210> 72 <211> 1752

260

Arg Pro Arg Ser Ser Asn Ala Glu Thr Leu Tyr

<212> PRT

<213> Homo Sapiens

<400> 72

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Thr	Arg	Leu	Arg 420	Ile	Asp	Tyr	Glu	Arg 425	Val	Ser	Gln	Glu	Arg 430	Thr	Val
Lys	Asp	Gln 435	Asp	Ile	Thr	Arg	Phe 440	Gln	Asn	Ser	Leu	Lys 445	Glu	Leu	Gln
	450					455					460		_	Arg	
465					470					475				Leu	480
				485					490					Asn 495	
			500					505					510	Glu	_
Asp	Leu	Arg 515	Gln	Gln	Arg	Asp	Val 520	Leu	Asp	Gly	His	Leu 525	Arg	Glu	Lys
	530					535					540			Glu	
545					550					555				Ala	560
				565					570					Arg 575	
			580					585					590	Thr	
		595					600					605	_	Asn	
	610					615					620			Asp	
625					630					635				Ile	640
				645					650					Gln 655	_
			660					665					670	Gln	
		675					680					685		Thr	
	690					695					700			Leu	
705					710					715				Arg	720
				725					730					Glu 735	_
			740					745					750	Gln	
		755					760					765		Glu	_
	770					775					780			Leu	
Ala 785	Glu	Ile	Lys	Arg	Ile 790	Glu	Glu	Arg	Cys	Arg 795	Arg	Lys	Leu	Glu	Asp 800
Ser	Thr	Arg	Glu	Thr 805	Gln	Ser	Gln	Leu	Glu 810	Thr	Glu	Arg	Ser	Arg 815	Tyr
			820					825					830	His	_
Glu	Thr	Gln 835	Thr	Glu	Cys	Glu	Trp 840	Thr	Val	Asp	Thr	Ser 845	Lys	Leu	Val

	850					855	Val				860				_
865					870		Leu			875					880
Ser	Val	Glu	Glu	Val 885	Ala	Ser	Glu	Ile	Gln 890	Pro	Phe	Leu	Arg	Gly 895	Ala
Gly	Ser	Ile	Ala 900	Gly	Ala	Ser	Ala	Ser 905	Pro	Lys	Glu	Lys	Tyr 910	Ser	Leu
		915					Leu 920					925			
Leu	Leu 930	Glu	Ala	Gln	Ala	Ala 935	Thr	Gly	Gly	Ile	Ile 940	Asp	Pro	His	Arg
Asn 945	Glu	Lys	Leu	Thr	Val 950	Asp	Ser	Ala	Ile	Ala 955	Arg	Asp	Leu	Ile	Asp 960
Phe	Asp	Asp	Arg	Gln 965	Gln	Ile	Tyr	Ala	Ala 970		Lys	Ala	Ile	Thr 975	
Phe	Asp	Asp	Pro 980	Phe	Ser	Gly	Lys	Thr 985	Val	Ser	Val	Ser	Glu 990	Ala	Ile
		995					Glu 1000)				1009	5		
	1010)				1019					1020)			
		Asp	Val	Ala	Leu	Ala	Arg	Gly	Leu	Ile	Asp	Arg	Asp	Leu	Tyr
1025					1030					1035	-				104
Arg	Ser	Leu	Asn	Asp 1045		Arg	Asp	Ser	Gln 1050		Asn	Phe	Val	Asp 1055	
Val	Thr	Lys	Lys 1060		Val	Ser	Tyr	Val 1069		Leu	Lys	Glu	Arg	_	Arg
Ile	Glu	Pro 1079	His		Gly	Leu	Leu 1080	Leu		Ser	Val		Lys		Ser
		1079 Phe	His	Thr			1080 Gln	Leu)	Leu		Val	1089 Thr	Lys	Arg	
Met	Ser 1090	1079 Phe O	His Gln	Thr Gly	Ile	Arg 109!	1080 Gln 5	Leu) Pro	Leu Val	Thr	Val	1089 Thr	Lys 5 Glu	Arg Leu	Val
Met	Ser 1090 Ser	1079 Phe O	His Gln	Thr Gly	Ile	Arg 109! Pro	1080 Gln	Leu) Pro	Leu Val	Thr	Val 1100 Glu	1089 Thr	Lys 5 Glu	Arg Leu	Val
Met Asp 110	Ser 1090 Ser	1079 Phe O Gly	His Gln Ile	Thr Gly Leu	Ile Arg	Arg 109! Pro	1080 Gln 5	Leu) Pro Thr	Leu Val Val	Thr Asn	Val 1100 Glu	1089 Thr) Leu	Lys Glu Glu	Arg Leu Ser	Val Gly 112
Met Asp 1109 Gln	Ser 1090 Ser Ile	1079 Phe O Gly Ser	His Gln Ile Tyr	Thr Gly Leu Asp 1125	Ile Arg 1110 Glu	Arg 109! Pro Val	1080 Gln Ser Ser	Leu Pro Thr	Leu Val Val Arg	Thr Asn 1113 Ile	Val 1100 Glu 5 Lys	1089 Thr Leu Asp	Lys Glu Glu Phe	Arg Leu Ser Leu 1135	Val Gly 112 Gln
Met Asp 1109 Gln	Ser 1090 Ser Ile	1079 Phe O Gly Ser	His Gln Ile Tyr	Thr Gly Leu Asp 1129 Ile	Ile Arg 1110 Glu	Arg 109! Pro Val	1080 Gln Ser	Leu Pro Thr Glu	Val Val Arg 1130 Asn	Thr Asn 1113 Ile	Val 1100 Glu 5 Lys	1089 Thr Leu Asp	Lys Glu Glu Phe Lys	Arg Leu Ser Leu 1135 Gln	Val Gly 112 Gln
Met Asp 1109 Gln Gly	Ser 1090 Ser Tle Ser	1079 Phe O Gly Ser	His Gln Ile Tyr Cys 1140	Thr Gly Leu Asp 1129 Ile	Ile Arg 1110 Glu Ala	Arg 1099 Pro Val Gly	1080 Gln Ser Gly	Leu Pro Thr Glu Tyr 114	Val Val Arg 1130 Asn	Thr Asn 111: Ile O Glu	Val 1100 Glu Lys Thr	1089 Thr D Leu Asp	Lys Glu Glu Phe Lys 1156	Arg Leu Ser Leu 1139 Gln	Val Gly 112 Gln 5 Lys
Met Asp 1109 Gln Gly	Ser 1090 Ser Tle Ser	1079 Phe O Gly Ser Ser	His Gln Ile Tyr Cys 1140 Tyr	Thr Gly Leu Asp 1129 Ile	Ile Arg 1110 Glu Ala	Arg 1099 Pro Val Gly	Gln Ser Gly Ile	Leu Pro Thr Glu Tyr 1149	Val Val Arg 1130 Asn	Thr Asn 111: Ile O Glu	Val 1100 Glu Lys Thr	Thr Leu Asp Thr	Lys Glu Glu Phe Lys 1156	Arg Leu Ser Leu 1139 Gln	Val Gly 112 Gln 5 Lys
Met Asp 1109 Gln Gly Leu	Ser 1090 Ser The Ser	1079 Phe Office Ser Ser Ile 1159	His Gln Ile Tyr Cys 1140 Tyr	Thr Gly Leu Asp 1129 Ile Glu	Arg 1110 Glu Ala	Arg 1099 Pro Val Gly Met	Ser Gly Ile	Leu) Pro Thr Glu Tyr 114! Ile	Val Val Arg 1130 Asn Gly	Thr Asn 1119 Ile O Glu Leu	Val 1100 Glu 5 Lys Thr	Thr Leu Asp Thr Arg	Lys Glu Glu Phe Lys 1156 Pro	Leu Ser Leu 1139 Gln Gly	Val Gly 112 Gln Lys Thr
Met Asp 1109 Gln Gly Leu	Ser 1090 Ser The Ser	1079 Phe Ofly Ser Ser Ile 1159 Glu	His Gln Ile Tyr Cys 1140 Tyr	Thr Gly Leu Asp 1129 Ile Glu	Arg 1110 Glu Ala	Arg 1099 Pro Val Gly Met	Ser Gly Ile Lys 1160 Gln	Leu) Pro Thr Glu Tyr 114! Ile	Val Val Arg 1130 Asn Gly	Thr Asn 1119 Ile O Glu Leu	Val 1100 Glu 5 Lys Thr	Thr Leu Asp Thr Arg 1169	Lys Glu Glu Phe Lys 1156 Pro	Leu Ser Leu 1139 Gln Gly	Val Gly 112 Gln Lys Thr
Met Asp 1109 Gln Gly Leu Ala	Ser 1090 Ser 5 Ile Ser Gly Leu	1079 Phe Gly Ser Ser Ile 1159 Glu	His Gln Ile Tyr Cys 1140 Tyr Leu	Thr Gly Leu Asp 1129 Ile Glu Leu	Arg 1110 Glu Ala Ala Glu	Arg 1099 Pro Val Gly Met Ala 1179	1080 Gln Ser Gly Ile Lys 1160 Gln	Leu Pro Thr Glu Tyr 114! Ile Ala	Val Val Arg 1130 Asn Gly Ala	Thr Asn 1119 Ile Glu Leu Thr	Val 1100 Glu Lys Thr Val Gly 1180	Thr Leu Asp Thr Arg 1169 Phe	Lys Glu Glu Phe Lys 1150 Pro Ile	Leu Ser Leu 1135 Gln Gly Val	Val Gly 112 Gln Lys Thr
Met Asp 1109 Gln Gly Leu Ala Pro 1189	Ser 1090 Ser 5 Ile Ser Gly Leu 1170 Val	1079 Phe Gly Ser Ser Ile 1159 Glu Ser	His Gln Ile Tyr Cys 1140 Tyr Leu Asn	Thr Gly Leu Asp 1129 Ile Glu Leu Leu	Arg 1110 Glu Ala Ala Glu Arg 1190	Arg 1099 Pro Val Gly Met Ala 1179 Leu	Gln Ser Gly Ile Lys 1160 Gln Fro	Leu Pro Thr Glu Tyr 1149 Ile Ala Val	Val Val Arg 1130 Asn Gly Ala Glu	Asn 111! Ile Glu Leu Thr Glu 119!	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala	1089 Thr Leu Asp Thr Arg 1169 Phe Tyr	Lys Glu Glu Phe Lys 1150 Pro Ile	Leu Ser Leu 1139 Gln Gly Val	Val Gly 112 Gln Lys Thr Asp Gly 120
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu	Ser 1090 Ser Ile Ser Gly Leu 1170 Val	Ser Ile 115: Glu Ser Gly	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile	Thr Gly Leu Asp 1129 Ile Glu Leu Leu Glu 1209	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe	Arg 1099 Pro Val Gly Met Ala 1179 Leu	Gln Ser Gly Ile Lys 1160 Gln Pro	Leu Pro Thr Glu Tyr 114! Ile Ala Val	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210	Thr Asn 1119 Glu Leu Thr Glu 1199 Leu 0	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala 5	1089 Thr Leu Asp Thr Arg 1169 Phe Tyr Ala	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu	Leu Ser Leu 1135 Gln Gly Val Arg Arg 1215	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu Val	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Val Thr	Ser Ser Ile 115: Glu Ser Gly Gly	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220	Thr Gly Leu Asp 1129 Ile Glu Leu Leu Glu 1209 Asn	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe Asp	Arg 1099 Pro Val Gly Met Ala 1179 Leu Lys	Glu Glu Glu Glu Glu Glu	Leu Pro Thr Glu Tyr 114! Ile Xal Lys Thr 122!	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210 Gly 5	Asn 1119 Glu Leu Thr Glu 1199 Leu O Asn	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala 5 Ser	1089 Thr Leu Asp Thr Arg 1169 Tyr Ala Ile	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230	Leu Ser Leu 1135 Gln Gly Val Arg 1215 Leu	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala 5
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu Val	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Val Thr	1079 Phe Gly Ser Ser Ile 1159 Glu Ser Gly Gly Met	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220 Asn	Thr Gly Leu Asp 1129 Ile Glu Leu Leu Glu 1209 Asn	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe Asp	Arg 1099 Pro Val Gly Met Ala 1179 Leu Lys	Glu Glu Glu Glu Glu Glu Glu Glu	Leu Pro Thr Glu Tyr 1149 Ile Ala Val Lys Thr 1229 Glu	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210 Gly 5	Asn 1119 Glu Leu Thr Glu 1199 Leu O Asn	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala 5 Ser	1089 Thr Leu Asp Thr Arg 1169 Tyr Ala Ile	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230	Leu Ser Leu 1135 Gln Gly Val Arg 1215 Leu	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu Val Gln	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Val Thr	1079 Phe Gly Ser Ser Ile 1159 Glu Ser Gly Gly Met 1239	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220 Asn	Thr Gly Leu Asp 1129 Ile Glu Leu Leu Glu 1209 Asn Lys	Arg 1110 Glu Ala Ala Glu Arg 1190 Phe Asp Glu	Arg 1099 Pro Val Gly Met Ala 1179 Leu Lys Pro	Glu Glu Glu Glu Glu Glu Glu Glu	Leu Pro Thr Glu Tyr 1149 Ile Val Lys Thr 1229 Glu	Val Val Arg 1130 Asn 6 Gly Ala Glu Leu 1210 Gly 5	Thr Asn 111! Ile Glu Leu Thr Glu 119! Leu O Asn	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala 5 Ser Ile	Thr Leu Asp Thr Arg 1169 Phe Tyr Ala Ile Gly 1249	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230 Ile	Leu Ser Leu 1135 Gln Gly Val Arg 1215 Leu Arg	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala 5 Phe Leu
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu Val Gln Leu	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Thr Ala Glu 1250	Ser Ser Ile 1155 Glu Ser Gly Met 123 Ala	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220 Asn Gln	Thr Gly Leu Asp 1129 Glu Leu Leu Glu 1209 Asn Clys Ile	Arg illo Glu Ala Ala Glu Arg illo Phe Glu Asp Glu Ala	Arg 1099 Pro Val Gly Met Ala 1179 Leu Lys Pro Leu Thr	Glu Glu Glu Glu Glu Glu Glu Glu	Leu Pro Thr Glu Tyr 114! Ile Ala Val Lys Thr 122! Glu Gly	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210 Gly 5 Lys Ile	Thr Asn 1119 Glu Leu Thr Glu 1199 Leu O Asn Gly Ile	Val 1100 Glu Lys Thr Val Gly 1180 Ala Ser Ile His Asp 1260	Thr Arg 1169 Phe Gly 1249 Pro	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230 Ile Lys	Leu Ser Leu 1139 Gly Val Arg 1219 Leu Arg Glu	Val Gly 112 Gln 5 Lys Thr Asp Gly 120 Ala 5 Phe Leu Ser
Met Asp 1109 Gln Gly Leu Ala Pro 1189 Leu Val Gln Leu	Ser 1090 Ser Ile Ser Gly Leu 1170 Val Thr Ala Glu 1250 Arg	Ser Ser Ile 1155 Glu Ser Gly Met 123 Ala	His Gln Ile Tyr Cys 1140 Tyr Leu Asn Ile Tyr 1220 Asn Gln	Thr Gly Leu Asp 1129 Glu Leu Leu Glu 1209 Asn Clys Ile	Arg ille Glu Ala Ala Glu Arg il9 Asp Glu Ala	Arg 1099 Pro Val Gly Met Ala 1179 Leu D Lys Pro Leu Thr 125 Ile	Glu Glu Glu Glu Glu Glu Glu Glu	Leu Pro Thr Glu Tyr 114! Ile Ala Val Lys Thr 122! Glu Gly	Val Val Arg 1130 Asn Gly Ala Glu Leu 1210 Gly 5 Lys Ile	Thr Asn 1119 Glu Leu Thr Glu 1199 Leu O Asn Gly Ile	Val 1100 Glu 5 Lys Thr Val Gly 1180 Ala 5 Ser Ile His Asp 1260 Gly	Thr Arg 1169 Phe Gly 1249 Pro	Lys Glu Glu Phe Lys 1150 Pro Ile Lys Glu Ser 1230 Ile Lys	Leu Ser Leu 1139 Gly Val Arg 1219 Leu Arg Glu	Val Gly 112 Gln Lys Thr Asp Gly 120 Ala 5 Phe Leu

	1285	129	0	1295
Phe Asp Pro Asn 130	0	1305		1310
Arg Cys Ile Lys 1315		1320	132	5
Glu Lys Lys 1330	Gln Val Gln 1335		Lys Asn Thr 1340	Leu Arg Lys
Arg Arg Val Val 1345	Ile Val Asp 1350	Pro Glu Thr	Asn Lys Glu 1355	Met Ser Val
Gln Glu Ala Tyr	Lys Lys Gly 1365	Leu Ile Asp 137		Phe Lys Glu 1375
Leu Cys Glu Gln 138		Trp Glu Glu 1385	Ile Thr Ile	Thr Gly Ser
Asp Gly Ser Thr 1395	Arg Val Val	Leu Val Asp 1400	Arg Lys Thr	
Tyr Asp Ile Gln 1410	Asp Ala Ile			
Phe Asp Gln Tyr 1425	Arg Ser Gly 1430	Ser Leu Ser	Leu Thr Gln 1435	Phe Ala Asp
Met Ile Ser Leu	Lys Asn Gly 1445	Val Gly Thr		Met Gly Ser 1455
Gly Val Ser Asp				
Lys Ile Ser Thr 1475	Ile Ser Ser	Val Arg Asn 1480	Leu Thr Ile	Arg Ser Ser
Ser Phe Ser Asp 1490	Thr Leu Glu 1495			
Asp Thr Glu Asn 1505	Leu Glu Lys 1510	Ile Ser Ile		Ile Glu Arg
Gly Ile Val Asp	Ser Ile Thr 1525	Gly Gln Arg	Leu Leu Glu	
Cys Thr Gly Gly 154				
Gln Asp Ala Val 1555	Ser Gln Gly		Gln Asp Met	Ala Thr Ser
Val Lys Pro Ala 1570	Gln Lys Ala 1575			
Lys Lys Lys Met 1585	Ser Ala Ala 1590	Glu Ala Val		Trp Leu Pro
Tyr Glu Ala Gly		Leu Glu Phe 161	Gln Tyr Leu	Thr Gly Gly 1615
Leu Val Asp Pro				
Arg Lys Gly Phe 1635	Ile Asp Gly		Gln Arg Leu 164	Gln Asp Thr
Ser Ser Tyr Ala 1650	Lys Ile Leu 1655	Thr Cys Pro		
Ser Tyr Lys Asp 1665				Ile Thr Gly
Leu Arg Leu Leu		Ser Val Ser	Ser Lys Gly	
Pro Tyr Asn Met	Ser Ser Ala			
Gly Ser Arg Ser 1715			Arg Ser Gly	Ser Arg Arg

Gly Ser Phe Asp Ala Thr Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser 1735 1740 Phe Ser Ser Ser Ile Gly His

<210> 73 <211> 1978 <212> PRT

<213> Homo Sapiens

<400> 73

Met Ser Arg Pro Arg Phe Asn Pro Arg Gly Asp Phe Pro Leu Gln Arg Pro Arg Ala Pro Asn Pro Ser Gly Met Arg Pro Pro Gly Pro Phe Met 25 Arg Pro Gly Ser Met Gly Leu Pro Arg Phe Tyr Pro Ala Gly Arg Ala 40 Arg Gly Ile Pro His Arg Phe Ala Gly Leu Glu Ser Tyr Gln Asn Met Gly Pro Gln Arg Met Asn Val Gln Val Thr Gln His Arg Thr Asp Pro 70 75 Arg Leu Thr Lys Glu Lys Leu Asp Phe His Glu Ala Gln Gln Lys Lys 90 Gly Lys Pro His Gly Ser Arg Trp Asp Asp Glu Pro His Ile Ser Ala Ser Val Ala Val Lys Gln Ser Ser Val Thr Gln Val Thr Glu Gln Ser 120 Pro Lys Val Gln Ser Arg Tyr Thr Lys Glu Ser Ala Ser Ser Ile Leu 135 Ala Ser Phe Gly Leu Ser Asn Glu Asp Leu Glu Glu Leu Ser Arg Tyr 150 155 Pro Asp Glu Gln Leu Thr Pro Glu Asn Met Pro Leu Ile Leu Arg Asp 165 170 Ile Arg Met Arg Lys Met Gly Arg Arg Leu Pro Asn Leu Pro Ser Gln 1.80 185 Ser Arg Asn Lys Glu Thr Leu Gly Ser Glu Ala Val Ser Ser Asn Val 200 Ile Asp Tyr Gly His Ala Ser Lys Tyr Gly Tyr Thr Glu Asp Pro Leu 215 Glu Val Arg Ile Tyr Asp Pro Glu Ile Pro Thr Asp Glu Val Glu Asn 235 Glu Phe Gln Ser Gln Gln Asn Ile Ser Ala Ser Val Pro Asn Pro Asn 245 250 Val Ile Cys Asn Ser Met Phe Pro Val Glu Asp Val Phe Arg Gln Met 265 Asp Phe Pro Gly Glu Ser Ser Asn Asn Arg Ser Phe Phe Ser Val Glu 280 Ser Gly Thr Lys Met Ser Gly Leu His Ile Ser Gly Gly Gln Ser Val 295 Leu Glu Pro Ile Lys Ser Val Asn Gln Ser Ile Asn Gln Thr Val Ser 310 315 Gln Thr Met Ser Gln Ser Leu Ile Pro Pro Ser Met Asn Gln Gln Pro 330 Phe Ser Ser Glu Leu Ile Ser Ser Val Ser Gln Gln Glu Arg Ile Pro

345

His	Glu	Pro 355	Val	Ile	Asn	Ser	Ser 360	Asn	Val	His	Val	Gly 365	Ser	Arg	Gly
Ser	Lys 370	Lys	Asn	Tyr	Gln	Ser 375	Gln	Ala	Asp	Ile	Pro 380	Ile	Arg	Ser	Pro
Phe 385	Gly	Ile	Val	Lys	Ala 390	Ser	Trp	Leu	Pro	Lys 395	Phe	Ser	His	Ala	Asp 400
Ala	Gln	Lys	Met	Lys 405	Arg	Leu	Pro	Thr	Pro 410	Ser	Met	Met	Asn	Asp 415	Tyr
Tyr	Ala	Ala	Ser 420	Pro	Arg	Ile	Phe	Pro 425	His	Leu	Cys	Ser	Leu 430	Cys	Asn
Val	Glu	Cys 435	Ser	His	Leu	Lys	Asp 440	Trp	Ile	Gln	His	Gln 445	Asn	Thr	Ser
Thr	His 450	Ile	Glu	Ser	Cys	Arg 455	Gln	Leu	Arg	Gln	Gln 460	Tyr	Pro	Asp	Trp
Asn 465	Pro	Glu	Ile	Leu	Pro 470	Ser	Arg	Arg	Asn	Glu 475	Gly	Asn	Arg	Lys	Glu 480
				485					490					Arg 495	
Arg	Arg	Ser	Ser 500	Ser	Ser	His	Arg	Phe 505	Arg	Arg	Ser	Arg	Ser 510	Pro	Met
	_	515	-	_		_	520	_			_	525	-	His	-
	530					535					540			Tyr	
Ile 545	Arg	Asn	Pro	Phe	Arg 550	Gly	Ser	Pro	Lys	Cys 555	Phe	Arg	Ser	Val	Ser 560
				565	_				570			_	_	Lys 575	_
			580					585	_		_		590	Phe	
		595					600					605		Ala	
_	610					615		_			620	_		Thr	
625					630					635				Cys	640
Ser	Lys	Asn	Leu	Glu 645	Asp	Asp	Thr	Leu	Ser 650	Glu	Cys	Lys	Gln	Val 655	Ser
			660					665			_		670	Ser	
	_	675					680					685	_	_	Cys
	690					695					700				Asn
705					710					715					Glu 720
				725					730					735	Pro
			740					745		_			750	-	Lys
		755					760					765			Lys
	770					775					780				Val
Glu	Ile	Val	Thr	Ser	Thr	Ser	Ala	Ala	Lys	Thr	Gly	Gln	Ala	Lys	Ala

785					790					795					800
Cys	Val	Ala	Lys	Val 805	Asn	Lys	Ser	Thr	Gly 810	Lys	Ser	Ala	Ser	Ser 815	Val
Lys	Ser	Val	Val 820	Thr	Val	Ala	Val	Lys 825	Gly	Asn	Lys	Ala	Ser 830	Ile	Lys
		835	Ser	_	-	-	840					845	-		-
Asn	Val 850	Lys	Asn	Lys	Asp	Ser 855	Asn	Lys	Pro	Val	Thr 860	Ile	Pro	Glu	Asn
Ser 865	Glu	Ile	Lys	Thr	Ser 870	Ile	Glu	Val	Lys	Ala 875	Thr	Glu	Asn	Cys	Ala 880
Lys	Glu	Ala	Ile	Ser 885	Asp	Ala	Ala	Leu	Glu 890	Ala	Thr	Glu	Asn	Glu 895	Pro
			Glu 900					905					910		
Pro	Asn	Lys 915	Gly	Tyr	Ser	Val	Glu 920	Glu	Val	Tyr	Asp	Leu 925	Ala	Lys	Pro
Phe	Gly 930	Gly	Leu	Lys	Asp	Ile 935	Leu	Ile	Leu	Ser	Ser 940	His	Lys	Lys	Ala
Tyr 945	Ile	Glu	Ile	Asn	Arg 950	Lys	Ala	Ala	Glu	Ser 955	Met	Val	Lys	Phe	Tyr 960
Thr	Cys	Phe	Pro	Val 965	Leu	Met	Asp	Gly	Asn 970	Gln	Leu	Ser	Ile	Ser 975	Met
			Asn 980				_	985					990		
Leu	Val	Lys 995	Glu	Asn	Asp	Pro	Glu 1000		Asn	Ile	Asp	Thr		Tyr	Asp
	101	0	His			101	5				102	0			
Leu 102		Val	Gly	Leu	Gln 103		Gly	Lys	Val	Asp 103		His	Val	Phe	Ile 104
Ser	Asn	Arg	Asn	Lys 104		Ile	Leu	Gln	Leu 105	_	Ser	Pro	Glu	Ser 105	
Gln	Ser	Met	Tyr 106		Phe	Leu	Lys	Gln 106		Pro	Gln	Asn	Ile 107	_	Asp
His	Met	Leu 107	Thr 5	Cys	Ser	Leu	Ser		Lys	Ile	Asp	Leu 108!		Glu	Val
Gln	Ile 109		His	Asp	Pro	Glu 109		Glu	Lys	Glu	Ser 110		Gly	Leu	Lys
		Pro	Ile	Asp			Glu	Val	Gln			Thr	Asp	Ser	Pro
110		Tara	Pro	λαn	111		C3.11	~1. ₁₁	G3.,,	111		Dwa	C	T 1.	112
261	val	цуз	PIO	112		пеп	Giu	GIU	113		1111	PIO	ser	113	
Thr	Glu	Thr	Leu 114	Val		Gln	Glu	Glu 114	Pro		Glu	Glu	Glu 115	Ala	Glu
Lys	Ala	Thr	Cys		Ser	Asp	Phe 116	Ala		Glu	Thr	Leu 116	Glu		Glu
Thr	Gln 117		Glu	Glu	Val	Lys 117		Glu	Ile	Pro	Leu 118	Val		Ser	Ala
Ser	Val	Ser	Ile	Glu	Gln			Glu	Asn	Ala			Cys	Ala	Leu
118		~-			119		_	_	~-	119					120
			Met	120	5				121	0				121	5
TTE	Asn	. Pro	Lys 122		Ala	Leu	. Leu	Pro 122		Asp	Ser	Val	Phe 123		Glu

Glu	Arg	Asn 1235	Leu 5	Lys	Gly	Ile	Leu 1240		Glu	Ser	Pro	Ser 1245		Ala	Glu
Asp	Phe 1250		Ser	Gly	Ile	Thr 1255		Thr	Met	Val	Glu 1260		Val	Ala	Glu
Val		Lys	Asn	Glu			Ser	Glu	Ile			Ser	Thr	Cys	
1265				_	1270				_	1275					128
Val	Thr	Leu	Val	Pro	Gly	Ile	Pro	Thr	Gly	Asp	Glu	Lys	Thr	Val	Asp
				1285					1290					1295	
Lys	Lys	Asn	Ile	Ser	Glu	Lys	Lys	Gly	Asn	Met	Asp	Glu	Lys	Glu	Glu
			1300			_	_	1305			_		1310		
Lys	Glu	Phe	Asn	Thr	Lvs	Glu	Thr			Asn	T.e.11	Gln			Thr
-1-		1315			-7~	U _U	1320			1100	шец	1325		O _T y	TILL
C3	T			T	7 ~~	<i>α</i> 1			N/	7	77.		-	** 7	a 7.
Glu			GIU	ьys	ASI			Arg	Mec	Asp			ьуs	val	Glu
	1330					1335					1340				
Lys	Met	Ala	Ala	Met	Lys	Glu	Lys	Pro	Ala	Glu	Asn	Thr	Leu	Phe	Lys
1345					1350)				1355	5				136
Ala	Tyr	Pro	Asn	Lys	Gly	Val	Gly	Gln	Ala	Asn	Lys	Pro	Asp	Glu	Thr
				1365					1370		_		-	1375	
Ser	Lvs	Thr	Ser	Tle	Leu	Ala	Va1	Ser			Ser	Ser	Ser		
			1380				• 44	1385		, u.		001	1390		110
200	TIA	T 7.70	Ala		т1.	7707	C 0 70			T	27-	*			77.7
Ser	116			vaı	тте	val			PIO	ьуя	Ala			THE	vaı
_	_	1395	-		_		1400					1405			
Ser			Glu	Asn	Gln	Lys	Ser	Phe	Pro	Lys	Ser	Val	Pro	Arg	Asp
	1410					1415					1420				
Gln	Ile	Asn	Ala	Glu	Lys	Lys	Leu	Ser	Ala	Lys	Glu	Phe	Gly	Leu	Leu
1425					1430)				1435	5				144
Lys	Pro	Thr	Ser	Ala	Ara	Ser	Glv	Leu	Ala	Glu	Ser	Ser	Ser	Lvs	Phe
*				1445			-		1450					1455	
Laze	Pro	Thr	Gln	Ser	Sar	T.e.r	ጥክጥ	2 x C	C137	C1337	Cor	C1337	A rece	Tla	602
Lys	Pro	Thr			Ser	Leu	Thr			Gly	Ser	Gly			Ser
			1460)				1465	5				1470)	
		Gln	1460 Gly)			Lys	1465 Leu	5			Asp	1470 Ile)	
Ala	Leu	Gln 147	1460 Gly) Lys	Leu	Ser	Lys 1480	1465 Leu)	Asp	Tyr	Arg	Asp	1470 Ile) Thr	Lys
Ala	Leu	Gln 147	1460 Gly) Lys	Leu	Ser	Lys 1480	1465 Leu)	Asp	Tyr	Arg	Asp	1470 Ile) Thr	Lys
Ala Gln	Leu Ser 1490	Gln 147! Gln	1460 Gly 5 Glu	Lys Thr	Leu Glu	Ser Ala 1495	Lys 1480 Arg	1469 Leu) Pro	Asp Ser	Tyr Ile	Arg Met	Asp 1489 Lys	1470 Ile 5 Arg	Thr Asp	Lys Asp
Ala Gln	Leu Ser 1490	Gln 147! Gln	1460 Gly	Lys Thr	Leu Glu	Ser Ala 1495	Lys 1480 Arg	1469 Leu) Pro	Asp Ser	Tyr Ile	Arg Met	Asp 1489 Lys	1470 Ile 5 Arg	Thr Asp	Lys Asp
Ala Gln Ser 1505	Leu Ser 1490 Asn	Gln 1479 Gln) Asn	1460 Gly Glu Lys	Lys Thr	Leu Glu Leu 1510	Ser Ala 1499 Ala	Lys 1480 Arg 5 Glu	1465 Leu) Pro Gln	Asp Ser Asn	Tyr Ile Thr 151	Arg Met 1500 Lys	Asp 1489 Lys) Asn	1470 Ile 5 Arg Pro	Thr Asp Lys	Lys Asp Ser 152
Ala Gln Ser 1505	Leu Ser 1490 Asn	Gln 1479 Gln) Asn	1460 Gly Glu Lys	Lys Thr	Leu Glu Leu 1510	Ser Ala 1499 Ala	Lys 1480 Arg 5 Glu	1465 Leu) Pro Gln	Asp Ser Asn	Tyr Ile Thr 151	Arg Met 1500 Lys	Asp 1489 Lys) Asn	1470 Ile 5 Arg Pro	Thr Asp Lys	Lys Asp Ser 152
Ala Gln Ser 1505	Leu Ser 1490 Asn	Gln 1479 Gln) Asn	1460 Gly 5 Glu	Lys Thr	Leu Glu Leu 1510 Ser	Ser Ala 1499 Ala	Lys 1480 Arg 5 Glu	1465 Leu) Pro Gln	Asp Ser Asn Glu	Tyr Ile Thr 1519 Glu	Arg Met 1500 Lys	Asp 1489 Lys) Asn	1470 Ile 5 Arg Pro	Thr Asp Lys Pro	Lys Asp Ser 152 Phe
Ala Gln Ser 1505 Thr	Leu Ser 1490 Asn Thr	Gln 1479 Gln) Asn Gly	Gly Glu Lys Arg	Lys Thr Thr Ser	Leu Glu Leu 1510 Ser	Ser Ala 1499 Ala) Lys	Lys 1480 Arg Glu Ser	1469 Leu Pro Gln Lys	Asp Ser Asn Glu 1530	Tyr Ile Thr 151! Glu	Arg Met 1500 Lys Pro	Asp 1489 Lys) Asn Leu	1470 Ile Arg Pro	Thr Asp Lys Pro 1535	Lys Asp Ser 152 Phe
Ala Gln Ser 1505 Thr	Leu Ser 1490 Asn Thr	Gln 1479 Gln) Asn Gly	Gly Glu Lys Arg	Lys Thr Thr Ser 1525	Leu Glu Leu 1510 Ser	Ser Ala 1499 Ala) Lys	Lys 1480 Arg Glu Ser	Lys Asp	Asp Ser Asn Glu 1530	Tyr Ile Thr 151! Glu	Arg Met 1500 Lys Pro	Asp 1489 Lys) Asn Leu	1470 Ile 5 Arg Pro Phe Glu	Thr Asp Lys Pro 1535	Lys Asp Ser 152 Phe
Ala Gln Ser 1505 Thr	Leu Ser 1490 Asn Thr	Gln 1479 Gln) Asn Gly Asp	Gly Glu Lys Arg Glu 1540	Thr Ser 1525 Phe	Leu Glu Leu 1510 Ser Val	Ser Ala 1499 Ala) Lys Thr	Lys 1480 Arg Glu Ser Val	Leu Pro Gln Lys Asp	Asp Ser Asn Glu 1530 Glu	Tyr Ile Thr 151! Glu Val	Arg Met 1500 Lys Pro	Asp 1489 Lys Asn Leu Glu	1470 Ile Arg Pro Phe Glu 1550	Thr Asp Lys Pro 1539 Val	Lys Asp Ser 152 Phe Asn
Ala Gln Ser 1505 Thr	Leu Ser 1490 Asn Thr	Gln 147! Gln Asn Gly Asp	Gly Glu Lys Arg Glu 1540 Ala	Thr Ser 1525 Phe	Leu Glu Leu 1510 Ser Val	Ser Ala 1499 Ala) Lys Thr	Lys 1480 Arg Glu Ser Val	Leu Pro Gln Lys Asp 1545 Leu	Asp Ser Asn Glu 1530 Glu	Tyr Ile Thr 151! Glu Val	Arg Met 1500 Lys Pro	Asp 1489 Lys Asn Leu Glu	1470 Ile 5 Arg Pro Phe Glu 1550 Lys	Thr Asp Lys Pro 1539 Val	Lys Asp Ser 152 Phe Asn
Ala Gln Ser 1505 Thr Asn Pro	Leu Ser 1490 Asn Thr Leu Ser	Gln 147! Gln Asn Gly Asp Gln 155!	Glu Lys Arg Glu 1540 Ala	Lys Thr Thr Ser 1525 Phe Lys	Leu Glu Leu 1510 Ser Val Gln	Ser Ala 1499 Ala) Lys Thr	Lys 1480 Arg Glu Ser Val Pro 1560	Leu Pro Gln Lys Asp 1549 Leu D	Asp Ser Asn Glu 1530 Glu Lys	Tyr Ile Thr 151! Glu Val	Arg Met 1500 Lys Fro Ile	Asp 1489 Lys Asn Leu Glu Arg 1569	1470 Ile 5 Arg Pro Phe Glu 1550 Lys	Thr Asp Lys Pro 1535 Val	Lys Asp Ser 152 Phe Asn Thr
Ala Gln Ser 1505 Thr Asn Pro	Leu Ser 1490 Asn Thr Leu Ser	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn	Gly Glu Lys Arg Glu 1540 Ala	Lys Thr Thr Ser 1525 Phe Lys	Leu Glu Leu 1510 Ser Val Gln	Ser Ala 1499 Ala Lys Thr Asn Ser	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu	Leu Pro Gln Lys Asp 1549 Leu D	Asp Ser Asn Glu 1530 Glu Lys	Tyr Ile Thr 151! Glu Val	Arg Met 1500 Lys Fro Ile	Asp 1489 Lys Asn Leu Glu Arg 1569	1470 Ile 5 Arg Pro Phe Glu 1550 Lys	Thr Asp Lys Pro 1535 Val	Lys Asp Ser 152 Phe Asn Thr
Ala Gln Ser 1505 Thr Asn Pro	Leu Ser 1490 Asn Thr Leu Ser Lys 1570	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn	Glu Lys Arg Glu 1540 Ala 5	Lys Thr Ser 1525 Phe Lys Pro	Leu Glu Leu 1510 Ser Val Gln Phe	Ala 1499 Ala Lys Thr Asn Ser 1579	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu	1465 Leu Pro Gln Lys Asp 1545 Leu	Asp Ser Asn Glu 1530 Glu Lys Asn	Tyr Ile Thr 151! Glu Val Gly Leu	Met 1500 Lys Pro Ile Lys Lys 1580	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys	1470 Ile Arg Pro Phe Glu 1550 Lys Lys	Thr Asp Lys Pro 153! Val Glu Lys	Lys Asp Ser 152 Phe Asn Thr
Ala Gln Ser 1505 Thr Asn Pro	Leu Ser 1490 Asn Thr Leu Ser Lys 1570	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn	Glu Lys Arg Glu 1540 Ala 5	Lys Thr Ser 1525 Phe Lys Pro	Leu Glu Leu 1510 Ser Val Gln Phe	Ala 1499 Ala Lys Thr Asn Ser 1579	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu	1465 Leu Pro Gln Lys Asp 1545 Leu	Asp Ser Asn Glu 1530 Glu Lys Asn	Tyr Ile Thr 151! Glu Val Gly Leu	Met 1500 Lys Pro Ile Lys Lys 1580	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys	1470 Ile Arg Pro Phe Glu 1550 Lys Lys	Thr Asp Lys Pro 153! Val Glu Lys	Lys Asp Ser 152 Phe Asn Thr
Ala Gln Ser 1505 Thr Asn Pro	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn	Glu Lys Arg Glu 1540 Ala	Lys Thr Ser 1525 Phe Lys Pro	Leu Glu Leu 1510 Ser Val Gln Phe	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu	1465 Leu Pro Gln Lys Asp 1545 Leu	Asp Ser Asn Glu 1530 Glu Lys Asn	Tyr Ile Thr 151! Glu Val Gly Leu	Met 1500 Lys Pro Ile Lys Lys 1580 Leu	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys	1470 Ile Arg Pro Phe Glu 1550 Lys Lys	Thr Asp Lys Pro 153! Val Glu Lys	Lys Asp Ser 152 Phe Asn Thr Gly
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser	1460 Gly Glu Lys Arg Glu 1540 Ala 5 Val	Lys Thr Ser 1525 Phe Lys Pro	Leu Glu Leu 1510 Ser Val Gln Phe Arg	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val	1465 Leu Pro Gln Lys Asp 1549 Leu Leu Glu	Asp Ser Asn Glu 1530 Glu Lys Asn	Tyr Ile Thr 151! Glu Val Gly Leu Glu 159!	Met 1500 Lys Pro Ile Lys Lys 1580 Leu	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys Ser	1470 Ile Arg Pro Phe Glu 1550 Lys Lys Phe	Thr Asp Lys Pro 1535 Val Glu Lys Val	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser	Glu Lys Arg Glu 1540 Ala 5	Thr Thr Ser 1525 Phe Lys Pro Pro Gly	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val	1465 Leu Pro Gln Lys Asp 1549 Leu Leu Glu	Asp Ser Asn Glu 1530 Glu Lys Asn Gly	Tyr Ile Thr 1519 Glu Val Gly Leu Glu 1599 Ala	Met 1500 Lys Pro Ile Lys Lys 1580 Leu	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys Ser	1470 Ile Arg Pro Phe Glu 1550 Lys Lys Phe	Thr Asp Lys Pro 1535 Val Glu Lys Val Ala	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr Asp	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu	Glu Lys Arg Glu 1540 Ala Val Thr	Lys Thr Thr Ser 1525 Phe Lys Pro Pro Gly 1605	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val Glu 6	1465 Leu Pro Gln Lys Asp 1549 Leu Glu Asp	Asp Ser Asn Glu 1530 Glu Lys Asn Gly	Tyr Ile Thr 1519 Glu Val Gly Leu 1599 Ala	Met 1500 Lys Pro Ile Lys Lys 1580 Leu 5	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys Ser His	1470 Ile Arg Pro Phe Glu 1550 Lys Lys Phe Lys	Thr Asp Lys Pro 1535 Val Glu Lys Val Ala 1615	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr Asp	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu	Glu Lys Arg Glu 1540 Ala Val Thr	Lys Thr Ser 1525 Phe Lys Pro Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val Glu 6	1465 Leu Pro Gln Lys Asp 1545 Leu Glu Asp Ile	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp	Tyr Ile Thr 1519 Glu Val Gly Leu 1599 Ala	Met 1500 Lys Pro Ile Lys Lys 1580 Leu 5	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys Ser His	1470 Ile Arg Pro Phe Glu 1550 Lys Lys Phe Leu Leu	Thr Asp Lys Pro 1539 Val Glu Lys Val Ala 1619 Asn	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr Asp	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val	Glu Lys Arg Glu 1540 Ala Val Thr Ile	Lys Thr Ser 1525 Phe Lys Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly Glu Glu	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val Glu Val	1465 Leu Pro Gln Lys Asp 1545 Leu Glu Asp Ile 1625	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp	Tyr Ile Thr 1519 Val Gly Leu Glu 1599 Ala Clu	Met 1500 Lys Pro Ile Lys 1580 Leu Ala	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys O Ser His	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Lys Lys Lys Lys Leu Leu 1630	Thr Asp Lys Pro 1535 Val Glu Lys Val Ala 1615 Asn	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr Asp	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val	Glu Lys Arg Glu 1540 Ala 5 Val Thr Ile Thr 1620 Val	Lys Thr Ser 1525 Phe Lys Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp	Ala 1499 Ala Lys Thr Asn Ser 1579 Gly Glu Glu	Lys 1480 Arg Glu Ser Val Pro 1560 Glu Val Glu Val Asn	1465 Leu Pro Gln Lys Asp 1545 Leu Glu Asp Ile 1625 Ser	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp	Tyr Ile Thr 1519 Val Gly Leu Glu 1599 Ala Clu	Met 1500 Lys Pro Ile Lys 1580 Leu Ala	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys O Ser His	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Lys Lys Lys Lys Leu Leu 1630	Thr Asp Lys Pro 1535 Val Glu Lys Val Ala 1615 Asn	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala Glu	Leu Ser 1490 Asn Thr Leu Ser 1570 Thr Asp Leu Glu	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val Met 163	Glu Lys Arg Glu 1540 Ala Val Thr Ile Thr 1620 Val	Lys Thr Thr Ser 1525 Phe Lys Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp Asn	Ala 1499 Ala Lys Thr Asn Ser 1579 Glu Glu Glu Ser	Lys 1480 Arg Glu Ser Val Pro 1560 Glu Val Glu Val Asn 1640	1465 Leu Pro Gln Lys Asp 1549 Leu Glu Asp Ile 1629 Ser	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp Leu	Tyr Ile Thr 1519 Glu Val Gly Leu Glu 1599 Ala Glu Phe	Met 1500 Lys Pro Ile Lys 1580 Leu Ala Glu	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys Ser His Glu Leu 1649	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Lys Lys Lys Leu Leu 1630 Asp	Thr Asp Lys Pro 1539 Val Glu Lys Val Ala 1619 Asn Glu	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met Leu
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala Glu	Leu Ser 1490 Asn Thr Leu Ser 1570 Thr Asp Leu Glu	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val Met 163	Glu Lys Arg Glu 1540 Ala 5 Val Thr Ile Thr 1620 Val	Lys Thr Thr Ser 1525 Phe Lys Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp Asn	Ala 1499 Ala Lys Thr Asn Ser 1579 Glu Glu Ser Ile	Lys 1480 Arg Glu Ser Val Pro 1560 Glu Val Glu Val Asn 1646 Ser	1465 Leu Pro Gln Lys Asp 1549 Leu Glu Asp Ile 1629 Ser	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp Leu	Tyr Ile Thr 1519 Glu Val Gly Leu Glu 1599 Ala Glu Phe	Met 1500 Lys Pro Ile Lys 1580 Leu Ala Glu	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys Ser His Glu Leu 1649	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Lys Lys Lys Leu Leu 1630 Asp	Thr Asp Lys Pro 1539 Val Glu Lys Val Ala 1619 Asn Glu	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met Leu
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala Glu	Leu Ser 1490 Asn Thr Leu Ser 1570 Thr Asp Leu Glu	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val Met 163 Gln	Glu Lys Arg Glu 1540 Ala Val Thr Ile Thr 1620 Val	Lys Thr Thr Ser 1525 Phe Lys Pro Gly 1605 Val	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp Asn	Ala 1499 Ala Lys Thr Asn Ser 1579 Glu Glu Glu Ser	Lys 1480 Arg Glu Ser Val Pro 1560 Glu Val Glu Val Asn 1646 Ser	1465 Leu Pro Gln Lys Asp 1549 Leu Glu Asp Ile 1629 Ser	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp Leu	Tyr Ile Thr 1519 Glu Val Gly Leu Glu 1599 Ala Glu Phe	Met 1500 Lys Pro Ile Lys 1580 Leu Ala Glu	Asp 1485 Lys Asn Leu Glu Arg 1565 Lys Ser His Glu Leu 1641 Lys	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Lys Lys Lys Leu Leu 1630 Asp	Thr Asp Lys Pro 1539 Val Glu Lys Val Ala 1619 Asn Glu	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met Leu
Ala Gln Ser 1505 Thr Asn Pro Leu Lys 1585 Leu Ala Glu Ile	Leu Ser 1490 Asn Thr Leu Ser Lys 1570 Thr Asp Leu Glu Asp 1650	Gln 1479 Gln Asn Gly Asp Gln 1559 Asn Ser Glu Val Met 163 Gln	Glu Lys Arg Glu 1540 Ala Val Thr Ile Thr 1620 Val	Lys Thr Ser 1525 Phe Lys Pro Gly 1605 Val Clys Asp	Leu Glu Leu 1510 Ser Val Gln Phe Arg 1590 Glu Asp Asn Cys	Ala 1499 Ala Lys Thr Asn Ser 1579 Glu Glu Glu Ser Ile 165	Lys 1480 Arg 5 Glu Ser Val Pro 1560 Glu 5 Val Glu Val Asn 1640 Ser 5	1465 Leu Pro Gln Lys Asp 1545 Leu Leu Glu Asp Ile 1625 Ser His	Asp Ser Asn Glu 1530 Glu Lys Asn Gly Ala 1610 Asp Leu Ser	Tyr Ile Thr 151! Glu Val Gly Leu Glu 159! Ala Glu Phe	Met 1500 Lys Pro Ile Lys 1580 Leu Ala Glu Thr	Asp 1489 Lys Asn Leu Glu Arg 1569 Lys Ser His Glu Leu 1649 Lys	1470 Ile The Arg Pro Phe Glu 1550 Lys Lys Leu 1630 Asp Asp	Thr Asp Lys Pro 1535 Val Glu Lys Val Ala 1615 Asn Glu Val	Lys Asp Ser 152 Phe Asn Thr Gly Thr 160 Gln Met Leu Thr

1665 1670 1675 Val Thr Val Asp Glu Ile Gly Glu Val Glu Glu Leu Pro Leu Asn Glu 1690 Ser Ala Asp Ile Thr Phe Ala Thr Leu Asn Thr Lys Gly Asn Glu Gly 1700 1705 Asp Ile Val Arg Asp Ser Ile Gly Phe Ile Ser Ser Gln Val Pro Glu 1715 1720 1725 Asp Pro Ser Thr Leu Val Thr Val Asp Glu Ile Gln Asp Asp Ser Ser 1735 1740 Asp Leu His Leu Val Thr Leu Asp Glu Val Thr Glu Glu Asp Glu Asp 1750 1755 Ser Leu Ala Asp Phe Asn Asn Leu Lys Glu Glu Leu Asn Phe Val Thr 1765 1770 Val Asp Glu Val Gly Glu Glu Glu Asp Gly Asp Asn Asp Leu Lys Val 1785 Glu Leu Ala Gln Ser Lys Asn Asp His Pro Thr Asp Lys Lys Gly Asn 1800 Arg Lys Lys Arg Ala Val Asp Thr Lys Lys Thr Lys Leu Glu Ser Leu 1815 1820 Ser Gln Val Gly Pro Val Asn Glu Asn Val Met Glu Glu Asp Leu Lys 1830 1835 Thr Met Ile Glu Arg His Leu Thr Ala Lys Thr Pro Thr Lys Arg Val 1850 1855 1845 Arg Ile Gly Lys Thr Leu Pro Ser Glu Lys Ala Val Val Thr Glu Pro 1860 1865 Ala Lys Gly Glu Glu Ala Phe Gln Met Ser Glu Val Asp Glu Glu Ser 1875 1880 1885 Gly Leu Lys Asp Ser Glu Pro Glu Arg Lys Arg Lys Lys Thr Glu Asp 1895 1900 Ser Ser Ser Gly Lys Ser Val Ala Ser Asp Val Pro Glu Glu Leu Asp 1910 1915 192 Phe Leu Val Pro Lys Ala Gly Phe Phe Cys Pro Ile Cys Ser Leu Phe 1925 1930 Tyr Ser Gly Glu Lys Ala Met Thr Asn His Cys Lys Ser Thr Arg His 1940 1945 Lys Gln Asn Thr Glu Lys Phe Met Ala Lys Gln Arg Lys Glu Lys Glu 1960 1965 Gln Asn Glu Ala Glu Glu Arg Ser Ser Arg 1970 1975

<210> 74

<211> 366

<212> PRT

<213> Homo Sapiens

<400> 74

 Met
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 Val
 Met
 Ala
 Pro
 Arg
 Thr
 Leu
 Ile
 Leu
 Leu
 Leu
 Ser
 Gly
 Ala

 Leu
 Ala
 Leu
 Thr
 Glu
 Thr
 Try
 Ala
 Gly
 Ser
 His
 Ser
 Met
 Arg
 Tyr
 Phe

 Tyr
 Thr
 Ala
 Val
 Ser
 Arg
 Pro
 Gly
 Arg
 Gly
 Glu
 Pro
 His
 Phe
 Ile
 Ala

 Val
 Gly
 Tyr
 Val
 Asp
 Asp
 Thr
 Gln
 Phe
 Val
 Arg
 Phe
 Asp
 Asp
 Ala

 50
 Tyr
 Val
 Gly
 Glu
 Pro
 Trp
 Val
 Glu
 65 70 75 Pro Glu Tyr Trp Asp Arg Glu Thr Gln Lys Tyr Lys Arg Gln Ala Gln 90 Thr Asp Arg Val Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser 100 105 Glu Ala Gly Ser His Ile Ile Gln Arg Met Tyr Gly Cys Asp Val Gly 120 Pro Asp Gly Arg Leu Leu Arg Gly Tyr Asp Gln Tyr Ala Tyr Asp Gly 135 140 Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala 150 Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu 165 170 Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Leu Cys Val Glu Trp Leu 185 Arg Arg Tyr Leu Lys Asn Gly Lys Glu Thr Leu Gln Arg Ala Glu His 200 Pro Lys Thr His Val Thr His His Pro Val Ser Asp His Glu Ala Thr 215 220 Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr 230 235 Trp Gln Trp Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu 245 250 Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val 265 Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu 275 280 Gly Leu Pro Glu Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Pro 295 300 Thr Ile Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val 310 Leu Ala Val Leu Gly Ala Val Val Ala Val Val Met Cys Arg Arg Lys 325 330 Ser Ser Gly Gly Lys Gly Gly Ser Cys Ser Gln Ala Ala Ser Ser Asn 345 Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Ala Cys Lys Ala 355 360

<210> 75

<211> 240

<212> PRT

<213> Homo Sapiens

<400> 75

 Met
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 Leu
 Glu
 Leu
 Tyr
 Leu
 Asp
 Leu
 Leu
 Ser
 Gln
 Pro
 Cys
 Arg
 Ala

 Val
 Tyr
 Ile
 Phe
 Ala
 Lys
 Lys
 Asp
 Ile
 Pro
 Phe
 Glu
 Leu
 Arg
 Ile

 Val
 Asp
 Leu
 Ile
 Lys
 Gly
 Gln
 His
 Leu
 Ser
 Asp
 Ala
 Phe
 Ala
 Gln
 Val

 Asp
 Pro
 Leu
 Lys
 Lys
 Val
 Rys
 Ala
 Leu
 Lys
 Asp
 Gly
 Asp
 Phe
 Thr
 Leu

 Asp
 Pro
 Leu
 Lys
 Asp
 Gly
 Asp
 Phe
 Thr
 Leu

 Asp
 Fro
 Leu
 Leu
 Leu
 Thr
 Leu
 Thr
 Arg
 Lys
 Thr
 Lys
 Thr
 Lys
 Thr
 Lys
 Lys
 Lys
 Lys

85 90 Glu Tyr Leu Ala Trp Gln His Thr Thr Leu Arg Arg Ser Cys Leu Arg 105 Ala Leu Trp His Lys Val Met Phe Pro Val Phe Leu Gly Gly Pro Val 120 Ser Pro Gln Thr Leu Ala Ala Thr Leu Ala Glu Leu Asp Val Thr Leu 135 140 Gln Leu Leu Glu Asp Lys Phe Leu Gln Asn Lys Ala Phe Leu Thr Gly 150 155 Pro His Ile Ser Leu Ala Asp Leu Val Ala Ile Thr Glu Leu Met His 165 170 Pro Val Gly Ala Gly Cys Gln Val Phe Glu Gly Arg Pro Lys Leu Ala 185 Thr Trp Arg Gln Arg Val Glu Ala Ala Val Gly Glu Asp Leu Phe Gln 200 Glu Ala His Glu Val Ile Leu Lys Ala Lys Asp Phe Pro Pro Ala Asp 215 220 Pro Thr Ile Lys Gln Lys Leu Met Pro Trp Val Leu Ala Met Ile Arg 235

<210> 76

<211> 953

<212> PRT

<213> Homo Sapiens

<400> 76

Met Ile Thr Ser Ala Ala Gly Ile Ile Ser Leu Leu Asp Glu Asp Glu 5 10 Pro Gln Leu Lys Glu Phe Ala Leu His Lys Leu Asn Ala Val Val Asn 25 Asp Phe Trp Ala Glu Ile Ser Glu Ser Val Asp Lys Ile Glu Val Leu 40 Tyr Glu Asp Glu Gly Phe Arg Ser Arg Gln Phe Ala Ala Leu Val Ala 55 60 Ser Lys Val Phe Tyr His Leu Gly Ala Phe Glu Glu Ser Leu Asn Tyr 70 Ala Leu Gly Ala Arg Asp Leu Phe Asn Val Asn Asp Asn Ser Glu Tyr 90 Val Glu Thr Ile Ile Ala Lys Cys Ile Asp His Tyr Thr Lys Gln Cys 105 Val Glu Asn Ala Asp Leu Pro Glu Gly Glu Lys Lys Pro Ile Asp Gln 120 Arg Leu Glu Gly Ile Val Asn Lys Met Phe Gln Arg Cys Leu Asp Asp 135 140 His Lys Tyr Lys Gln Ala Ile Gly Ile Ala Leu Glu Thr Arg Arg Leu 150 155 Asp Val Phe Glu Lys Thr Ile Leu Glu Ser Asn Asp Val Pro Gly Met 165 170 Leu Ala Tyr Ser Leu Lys Leu Cys Met Ser Leu Met Gln Asn Lys Gln 185 Phe Arg Asn Lys Val Leu Arg Val Leu Val Lys Ile Tyr Met Asn Leu 200 Glu Lys Pro Asp Phe Ile Asn Val Cys Gln Cys Leu Ile Phe Leu Asp 215 220 Asp Pro Gln Ala Val Ser Asp Ile Leu Glu Lys Leu Val Lys Glu Asp

225					230					235					240
			Met	245					250					255	
Ser	Gln	Gln	Phe 260	Leu	Ser	Ser	Val	Ile 265	Gln	Asn	Leu	Arg	Thr 270	Val	Gly
		275	Ala				280					285			
Gly	Ser 290	Glu	Lys	Asp	Ser	Asp 295	Ser	Met	Glu	Thr	Glu 300	Glu	Lys	Thr	Ser
305			Val		310					315				_	320
Gln	Thr	Leu	Lys	Met 325	Ile	Lys	Ile	Leu	Ser 330	Gly	Glu	Met	Ala	Ile 335	Glu
			Gln 340					345					350		
Leu	Lys	Asn 355	Thr	Lys	Asp	Ala	Val 360	Arg	Asn	Ser	Val	Cys 365	His	Thr	Ala
	370		Ala			375					380				
385			Asp		390					395					400
Lys	Phe	Thr	Ala	Thr 405	Ala	Ser	Leu	Gly	Val 410	Ile	His	Lys	Gly	His 415	Glu
			Leu 420					425					430		
Pro	Gly	Ser 435	Ala	Tyr	Gln	Glu	Gly 440	Gly	Gly	Leu	Tyr	Ala 445	Leu	Gly	Leu
Ile	His 450	Ala	Asn	His	Gly	Gly 455	Asp	Ile	Ile	Asp	Tyr 460	Leu	Leu	Asn	Gln
Leu 465	Lys	Asn	Ala	Ser	Asn 470	Asp	Ile	Val	Arg	His 475	Gly	Gly	Ser	Leu	Gly 480
			Ala	485					490					495	
			Asn 500					505					510		
Gly	Leu	Ala 515	Leu	Gly	Leu	Val	Met 520	Leu	Gly	Ser	Lys	Asn 525	Ala	Gln	Ala
	530		Met			535					540				
Leu 545	Arg	Gly	Leu	Ala	Val 550	Gly	Ile	Ala	Leu	Val 555	Met	Tyr	Gly	Arg	Met 560
Glu	Glu	Ala	Asp	Ala 565	Leu	Ile	Glu	Ser	Leu 570	Cys	Arg	Asp	Lys	Asp 575	Pro
Ile	Leu	Arg	Arg 580	Ser	Gly	Met	Tyr	Thr 585	Val	Ala	Met	Ala	T yr 590	Cys	Gly
Ser	Gly	Asn 595	Asn	Lys	Ala	Ile	Arg 600	Arg	Leu	Leu	His	Val 605	Ala	Val	Ser
Asp	Val 610	Asn	Asp	Asp	Val	Arg 615	Ser	Ala	Ala	Val	Glu 620	Ser	Leu	Gly	Phe
Ile 625	Leu	Phe	Arg	Thr	Pro 630	Glu	Gln	Cys	Pro	Ser 635	Val	Val	Ser	Leu	Leu 640
Ser	Glu	Ser	Tyr	Asn 645		His	Val	Arg	Tyr 650		Ala	Ala	Met	Ala 655	
Gly	Ile	Cys	Cys 660	Ala	Gly	Thr	Gly	Asn 665		Glu	Ala	Ile	Asn 670		Leu

Glu Pro Met Thr Asn Asp Pro Val Asn Tyr Val Arg Gln Gly Ala Leu 680 Ile Ala Ser Ala Leu Ile Met Ile Gln Gln Thr Glu Ile Thr Cys Pro 695 Lys Val Asn Gln Phe Arg Gln Leu Tyr Ser Lys Val Ile Asn Asp Lys 710 715 His Asp Asp Val Met Ala Lys Phe Gly Ala Ile Leu Ala Gln Gly Ile 730 Leu Asp Ala Gly Gly His Asn Val Thr Ile Ser Leu Gln Ser Arg Thr 740 745 Gly His Thr His Met Pro Ser Val Val Gly Val Leu Val Phe Thr Gln 760 Phe Trp Phe Trp Phe Pro Leu Ser His Phe Leu Ser Leu Ala Tyr Thr 775 Pro Thr Cys Val Ile Gly Leu Asn Lys Asp Leu Lys Met Pro Lys Val 790 795 Gln Tyr Lys Ser Asn Cys Lys Pro Ser Thr Phe Ala Tyr Pro Ala Pro 805 810 Leu Glu Val Pro Lys Glu Lys Glu Lys Glu Lys Val Ser Thr Ala Val Leu Ser Ile Thr Ala Lys Ala Lys Lys Lys Glu Lys Glu Lys 835 840 Lys Glu Glu Lys Met Glu Val Asp Glu Ala Glu Lys Lys Glu Glu 855 860 Lys Glu Lys Lys Glu Pro Glu Pro Asn Phe Gln Leu Leu Asp Asn 870 875 Pro Ala Arg Val Met Pro Ala Gln Leu Lys Val Leu Thr Met Pro Glu 885 890 Thr Cys Arg Tyr Gln Pro Phe Lys Pro Leu Ser Ile Gly Gly Ile Ile 900 905 Ile Leu Lys Asp Thr Ser Glu Asp Ile Glu Glu Leu Val Glu Pro Val 920 Ala Ala His Gly Pro Lys Ile Glu Glu Glu Glu Glu Pro Glu Pro 935 Pro Glu Pro Phe Glu Tyr Ile Asp Asp 945 950

<210> 77

<211> 335

<212> PRT

<213> Homo Sapiens

<400> 77

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 Lys
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 Gly
 Val
 Asn
 Gly
 Phe
 Gly
 Arg
 Ile
 Gly
 Arg
 Ala
 Ala
 Phe
 Asn
 Ser
 Gly
 Lys
 Val
 Asp
 Ile
 Val
 Ala
 Ala
 Ala
 Asn
 Ser
 Gly
 Lys
 Val
 Asp
 Ile
 Val
 Ala
 Ala</th

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Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu
           100
                               105
Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro Ser Ala Asp Ala
                          120
Pro Met Phe Val Met Gly Val Asn His Glu Lys Tyr Asp Asn Ser Leu
                       135
Lys Ile Ile Ser Asn Ala Ser Cys Thr Thr Asn Cys Leu Ala Pro Leu
                   150
                                      155
Ala Lys Val Ile His Asp Asn Phe Gly Ile Val Glu Gly Leu Met Thr
                                   170
Thr Val His Ala Ile Thr Ala Thr Gln Lys Thr Val Asp Gly Pro Ser
                               185
Gly Lys Leu Trp Arg Asp Gly Arg Gly Ala Leu Gln Asn Ile Ile Pro
                           200
Ala Ser Thr Gly Ala Ala Lys Ala Val Gly Lys Val Ile Pro Glu Leu
                       215
Asn Gly Lys Leu Thr Gly Met Ala Phe Arg Val Pro Thr Ala Asn Val
                   230
                                       235
Ser Val Val Asp Leu Thr Cys Arg Leu Glu Lys Pro Ala Lys Tyr Asp
               245
                                   250
Asp Ile Lys Lys Val Val Lys Gln Ala Ser Glu Gly Pro Leu Lys Gly
                               265
Ile Leu Gly Tyr Thr Glu His Gln Val Val Ser Ser Asp Phe Asn Ser
       275
                           280
Asp Thr His Ser Ser Thr Phe Asp Ala Gly Ala Gly Ile Ala Leu Asn
                       295
                                           300
Asp His Phe Val Lys Leu Ile Ser Trp Tyr Asp Asn Glu Phe Gly Tyr
                   310
                           315
Ser Asn Arg Val Val Asp Leu Met Ala His Met Ala Ser Lys Glu
                                   330
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<210> 78

<211> 117

<212> PRT

<213> Homo Sapiens

<400> 78

 Met
 Val
 Gln
 Arg
 Leu
 Thr
 Tyr
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 Arg
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 Jo
 Leu
 Ser
 Ala

 Ser
 Asn
 Lys
 Thr
 Arg
 Leu
 Ser
 Arg
 Thr
 Pro
 Gly
 Asn
 Arg
 Ile
 Val
 Tyr

 Leu
 Tyr
 Thr
 Lys
 Lys
 Val
 Gly
 Lys
 Ala
 Pro
 Lys
 Ala
 Cys
 Gly
 Val

 Cys
 Pro
 Gly
 Lys
 Lys
 Arg
 Pro
 Val
 Arg
 Pro
 Lys
 Pro
 Lys
 Pro
 Lys
 Int
 Lys
 Int
 In

Ser Gln Lys Ala Lys

115

<210> 79

<211> 614

<212> PRT

<213> Homo Sapiens

<400> 79

Arg Ser Gly Gln Pro Arg Ala Glu Gly Leu Gly Ala Gly Ala Gly 10 Pro Leu Arg Ala Met Ala Ala Pro Val Lys Gly Asn Arg Lys Gln Ser Thr Glu Gly Asp Ala Leu Asp Pro Pro Ala Ser Pro Lys Pro Ala Gly 40 Lys Gln Asn Gly Ile Gln Asn Pro Ile Ser Leu Glu Asp Ser Pro Glu 55 Ala Gly Gly Glu Arg Glu Glu Glu Glu Glu Arg Glu Glu Glu Gln Ala Phe Leu Val Ser Leu Tyr Lys Phe Met Lys Glu Arg His Thr Pro Ile 90 Glu Arg Val Pro His Leu Gly Phe Lys Gln Ile Asn Leu Trp Lys Ile 100 105 Tyr Lys Ala Val Glu Lys Leu Gly Ala Tyr Glu Leu Val Thr Gly Arg 120 Arg Leu Trp Lys Asn Val Tyr Asp Glu Leu Gly Gly Ser Pro Gly Ser 135 140 Thr Ser Ala Ala Thr Cys Thr Arg Arg His Tyr Glu Arg Leu Val Leu 150 155 Pro Tyr Val Arg His Leu Lys Gly Glu Asp Asp Lys Pro Leu Pro Thr 165 170 Ser Lys Pro Arg Lys Gln Tyr Lys Met Ala Lys Glu Asn Arg Gly Asp 185 Asp Gly Ala Thr Glu Arg Pro Lys Lys Ala Lys Glu Glu Arg Arg Met 200 Asp Gln Met Met Pro Gly Lys Thr Lys Ala Asp Ala Ala Asp Pro Ala 215 220 Pro Leu Pro Ser Gln Glu Pro Pro Arg Asn Ser Thr Glu Gln Gly 230 235 Leu Ala Ser Gly Ser Ser Val Ser Phe Val Gly Ala Ser Gly Cys Pro 245 250 Glu Ala Tyr Lys Arg Leu Leu Ser Ser Phe Tyr Cys Lys Gly Thr His Gly Ile Met Ser Pro Leu Ala Lys Lys Lys Leu Leu Ala Gln Val Ser 280 Lys Val Glu Ala Leu Gln Cys Gln Glu Glu Gly Cys Arg His Gly Ala 295 300 Glu Pro Gln Ala Ser Pro Ala Val His Leu Pro Glu Ser Pro Gln Ser 310 315 Pro Lys Gly Leu Thr Glu Asn Ser Arg His Arg Leu Thr Pro Gln Glu 325 330 Gly Leu Gln Ala Pro Gly Gly Ser Leu Arg Glu Glu Ala Gln Ala Gly Pro Cys Pro Ala Ala Pro Ile Phe Lys Gly Cys Phe Tyr Thr His Pro 360 Thr Glu Val Leu Lys Pro Val Ser Gln His Pro Arg Asp Phe Phe Ser 375 380 Arg Leu Lys Asp Gly Val Leu Leu Gly Pro Pro Gly Lys Glu Gly Leu 395

Ser Val Lys Glu Pro Gln Leu Val Trp Gly Gly Asp Ala Asn Arg Pro 405 410 Ser Ala Phe His Lys Gly Gly Ser Arg Lys Gly Ile Leu Tyr Pro Lys 425 Pro Lys Ala Cys Trp Val Ser Pro Met Ala Lys Val Pro Ala Glu Ser 440 Pro Thr Leu Pro Pro Thr Phe Pro Ser Ser Pro Gly Leu Gly Ser Lys 455 460 Arg Ser Leu Glu Glu Glu Gly Ala Ala His Ser Gly Lys Arg Leu Arg 475 Ala Val Ser Pro Phe Leu Lys Glu Ala Asp Ala Lys Lys Cys Gly Ala 485 490 Lys Pro Ala Gly Ser Gly Leu Val Ser Cys Leu Leu Gly Pro Ala Leu 505 Gly Pro Val Pro Pro Glu Ala Tyr Arg Gly Thr Met Leu His Cys Pro 520 Leu Asn Phe Thr Gly Thr Pro Gly Pro Leu Lys Gly Gln Ala Ala Leu 535 Pro Phe Ser Pro Leu Val Ile Pro Ala Phe Pro Ala His Phe Leu Ala 550 555 Thr Ala Gly Pro Ser Pro Met Ala Ala Gly Leu Met His Phe Pro Pro 565 570 Thr Ser Phe Asp Ser Ala Leu Arg His Arg Leu Cys Pro Ala Ser Ser 585 Ala Trp His Ala Pro Pro Val Thr Thr Tyr Ala Ala Pro His Phe 595 600 His Leu Asn Thr Lys Leu 610 <210> 80 <211> 114 <212> PRT <213> Homo Sapiens <400> 80 Met Ala Ser Val Ser Glu Leu Ala Cys Ile Tyr Ser Ala Leu Ile Leu His Asp Asp Glu Val Thr Val Thr Glu Asp Lys Ile Asn Ala Leu Ile Lys Ala Ala Gly Val Asn Val Glu Pro Phe Trp Pro Gly Leu Phe Ala 40 Lys Ala Leu Ala Asn Val Asn Ile Gly Ser Leu Ile Cys Asn Val Gly 55 Ala Gly Gly Pro Ala Pro Ala Ala Gly Ala Ala Pro Ala Gly Gly Pro 70 75 Ala Pro Ser Thr Ala Ala Ala Pro Ala Glu Glu Lys Lys Val Glu Ala 90 Lys Lys Glu Glu Ser Glu Glu Ser Asp Asp Met Gly Phe Gly Leu 105 Phe Asp

<210> 81

<211> 596

<212> PRT

<213> Homo Sapiens

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Asp Arg Pro Ala Asp Glu Tyr Asp Gln Pro Trp Glu Trp Asn Arg Val 425 Thr Ser Pro Ala Leu Ala Ala Gln Phe Asn Gly Asn Glu Lys Arg Gln 440 Ser Ser Pro Ser Pro Ser Arg Asp Arg Arg Arg Gln Leu Arg Ala Pro 455 460 Gly Gly Phe Lys Pro Ile Lys His Gly Ser Pro Glu Phe Cys Gly 470 475 Ile Leu Gly Glu Arg Val Asp Pro Ala Val Pro Leu Glu Lys Gln Ile 485 490 Trp Tyr His Gly Ala Ile Ser Arg Gly Asp Ala Glu Asn Leu Leu Arg 505 Leu Cys Lys Glu Cys Ser Tyr Leu Val Arg Asn Ser Gln Thr Ser Lys 515 520 His Asp Tyr Pro Leu Ser Leu Arg Ser Asn Gln Gly Phe Met His Met 535 540 Lys Leu Ala Lys Thr Lys Glu Lys Tyr Val Leu Gly Gln Asn Ser Pro 550 555 Pro Phe Asp Ser Val Pro Glu Val Ile His Tyr Tyr Thr Thr Arg Lys 565 570 Leu Pro Ile Lys Gly Ala Glu His Leu Ser Leu Leu Tyr Pro Val Ala 585 Val Arg Thr Leu 595

<210> 82

<211> 207

<212> PRT

<213> Homo Sapiens

<400> 82

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Ala Ala Asp Ala Ala Aser Ser Val Ala Lys Gly Gly Ala 195 200 205

<210> 83

<211> 429

<212> PRT

<213> Homo Sapiens

<400> 83

Glu Cys Asp Val Met Thr Tyr Val Arg Glu Thr Cys Gly Cys Cys Asp Cys Glu Lys Arg Cys Gly Ala Leu Asp Val Val Phe Val Ile Asp Ser 25 Ser Glu Ser Ile Gly Tyr Thr Asn Phe Thr Leu Glu Lys Asn Phe Val 40 Ile Asn Val Val Asn Arg Leu Gly Ala Ile Ala Lys Asp Pro Lys Ser 55 Glu Thr Gly Thr Arg Val Gly Val Val Gln Tyr Ser His Glu Gly Thr Phe Glu Ala Ile Gln Leu Asp Asp Glu His Ile Asp Ser Leu Ser Ser 85 90 Phe Lys Glu Ala Val Lys Asn Leu Glu Trp Ile Ala Gly Gly Thr Trp 105 Thr Pro Ser Ala Leu Lys Phe Ala Tyr Asp Arg Leu Ile Lys Glu Ser Arg Arg Gln Lys Thr Arg Val Phe Ala Val Val Ile Thr Asp Gly Arg 135 His Asp Pro Arg Asp Asp Leu Asn Leu Arg Ala Leu Cys Asp Arg 150 155 Asp Val Thr Val Thr Ala Ile Gly Ile Gly Asp Met Phe His Glu Lys 165 170 His Glu Ser Glu Asn Leu Tyr Ser Ile Ala Cys Asp Lys Pro Gln Gln 180 185 Val Arg Asn Met Thr Leu Phe Ser Asp Leu Val Ala Glu Lys Phe Ile 200 195 Asp Asp Met Glu Asp Val Leu Cys Pro Asp Pro Gln Ile Val Cys Pro 215 Asp Leu Pro Cys Gln Thr Glu Leu Ser Val Ala Gln Cys Thr Gln Arg 230 235 Pro Val Asp Ile Val Phe Leu Leu Asp Gly Ser Glu Arg Leu Gly Glu 250 Gln Asn Phe His Lys Ala Arg Arg Phe Val Glu Gln Val Ala Arg Arg 265 Leu Thr Leu Ala Arg Arg Asp Asp Asp Pro Leu Asn Ala Arg Val Ala 280 Leu Leu Gln Phe Gly Gly Pro Gly Glu Gln Gln Val Ala Phe Pro Leu 295 300 Ser His Asn Leu Thr Ala Ile His Glu Ala Leu Glu Thr Thr Gln Tyr 310 315 Leu Asn Ser Phe Ser His Val Gly Ala Gly Val Val His Ala Ile Asn 330 Ala Ile Val Arg Ser Pro Arg Gly Gly Ala Arg Arg His Ala Glu Leu

Ser Phe Val Phe Leu Thr Asp Gly Val Thr Gly Asn Asp Ser Leu His 355 360 365

<210> 84

<211> 113

<212> PRT

<213> Homo Sapiens

<400> 84

 Met
 Ser
 Ala
 Ser
 Val
 Ser
 Val
 Ile
 Ser
 Arg
 Phe
 Leu
 Glu
 Glu
 Tyr

 Leu
 Ser
 Thr
 Pro
 Gln
 Arg
 Leu
 Leu
 Leu
 Asp
 Ala
 Tyr
 Leu
 Val
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 Gly
 Phe
 Ile
 Ser
 Leu
 Leu
 Val
 Val
 Leu
 Ser
 Gly
 Phe
 Ile
 Ser
 Cys
 Val
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Gly

<211> 258

<212> PRT

<213> Homo Sapiens

<400> 85

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130 135 140 Ile Gly Gln Ser Leu Phe Asp Tyr Leu His Pro Lys Asp Ile Ala Lys 150 155 Val Lys Glu Gln Leu Ser Ser Ser Asp Thr Ala Pro Arg Glu Arg Leu 165 170 Ile Asp Ala Lys Thr Gly Leu Pro Val Lys Thr Asp Ile Thr Pro Gly 185 Pro Ser Arg Leu Cys Ser Gly Ala Arg Arg Ser Phe Phe Cys Arg Met 195 200 Lys Cys Asn Arg Pro Ser Val Asn Val Glu Asp Lys Asn Phe Pro Ser 215 220 Thr Cys Ser Lys Lys Lys Ala Asp Arg Lys Ala Phe Cys Thr Ile His 235 Ser Thr Gly Tyr Phe Gly Ile Phe Thr Thr Arg Thr Ser Arg His Ile 250 Val Leu

<210> 86 <211> 569 <212> PRT

<213> Homo Sapiens

<400> 86

Met Ser Thr Met Val Tyr Ile Lys Glu Asp Lys Leu Glu Lys Leu Thr Gln Asp Glu Ile Ile Ser Lys Thr Lys Gln Val Ile Gln Gly Leu Glu 25 Ala Leu Lys Asn Glu His Asn Ser Ile Leu Gln Ser Leu Leu Glu Thr 40 Leu Lys Cys Leu Lys Lys Asp Glu Ser Asn Leu Val Glu Glu Lys Ser Asn Met Ile Arg Lys Ser Leu Glu Met Leu Glu Leu Gly Leu Ser 70 75 Glu Ala Gln Val Met Met Ala Leu Ser Asn His Leu Asn Ala Val Glu 85 90 Ser Glu Lys Gln Lys Leu Arg Ala Gln Val Arg Arg Leu Cys Gln Glu 105 Asn Gln Trp Leu Arg Asp Glu Leu Ala Asn Thr Gln Gln Lys Leu Gln Lys Ser Glu Gln Ser Val Ala Gln Leu Glu Glu Glu Lys Lys His Leu 135 Glu Phe Met Asn Gln Leu Lys Lys Tyr Asp Asp Ile Ser Pro Ser 155 Glu Asp Lys Asp Thr Asp Ser Thr Lys Glu Pro Leu Asp Asp Leu Phe 170 165 Pro Asn Asp Glu Asp Asp Pro Gly Gln Gly Ile Gln Gln Gln His Ser 185 Ser Ala Ala Ala Ala Gln Gln Gly Gly Tyr Glu Ile Pro Ala Arg 200 Leu Arg Thr Leu His Asn Leu Val Ile Gln Tyr Ala Ser Gln Gly Arg 215 Tyr Glu Val Ala Val Pro Leu Cys Lys Gln Ala Leu Glu Asp Leu Glu 235 Lys Thr Ser Gly His Asp His Pro Asp Val Ala Thr Met Leu Asn Ile

				245					250					255	
Leu	Ala	Leu	Val 260	Tyr	Arg	Asp	Gln	Asn 265	Lys	Tyr	Lys	Asp	Ala 270	Ala	Asn
Leu	Leu	Asn 275	Asp	Ala	Leu	Ala	Ile 280	Arg	Glu	Lys	Thr	Leu 285	Gly	Lys	Asp
His	Pro 290	Ala	Val	Ala	Ala	Thr 295	Leu	Asn	Asn	Leu	Ala 300	Val	Leu	Tyr	Gly
Lys 305	Arg	Gly	Lys	Tyr	Lys 310	Glu	Ala	Glu	Pro	Leu 315	Cys	Lys	Arg	Ala	Leu 320
Glu	Ile	Arg	Glu	Lys 325	Val	Leu	Gly	Lys	Asp 330	His	Pro	Asp	Val	Ala 335	Lys
Gln	Leu	Asn	Asn 340	Leu	Ala	Leu	Leu	Cys 345	Gln	Asn	Gln	Gly	Lys 350	Tyr	Glu
Glu	Val	Glu 355	Tyr	Tyr	Tyr	Gln	Arg 360	Ala	Leu	Glu	Ile	Tyr 365	Gln	Thr	Lys
	370		Asp			375					380				
Ser 385	Cys	Tyr	Leu	Lys	Gln 390	Gly	Lys	Phe	Lys	Gln 395	Ala	Glu	Thr	Leu	Tyr 400
Lys	Glu	Ile	Leu	Thr 405	Arg	Ala	His	Glu	Arg 410	Glu	Phe	Gly	Ser	Val 415	Asp
			Lys 420					425					430		-
		435	Gln				440					445	_	_	-
	450		Cys			455					460				_
465			Ala		470					475					480
			Glu	485					490					495	
			Gln 500					505					510		
		515	Arg				520					525			_
	530		Pro			535					540				_
545			Val		550				Phe	Cys 5 5 5	Gly	Lys	Arg	Gln	Gln 560
Gln	Gln	Trp	Pro	Gly 565	Arg	Arg	His	Arg							

<210> 87

<211> 736

<212> PRT

<213> Homo Sapiens

<400> 87

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 Pro
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 Ile
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 Lys
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 Asp
 Val
 Phe
 Asn

 Thr
 Val
 Gly
 Ala
 Asp
 Ile
 Ile
 Gln
 Leu
 Pro
 Gln
 Ile
 Val
 Val
 Val
 Gly
 Gly
 Gly
 Arg
 Arg
 Arg
 Arg
 Arg
 Ile
 Ile
 Val
 Ile
 I

	50					55					60				
Leu 65	Gln	Leu	Val	His	Val 70	Thr	Gln	Glu	Asp	Lys 75	Arg	Lys	Thr	Thr	Gly 80
Glu	Glu	Asn	Gly	Val 85	Glu	Ala	Glu	Glu	Trp 90	Gly	Lys	Phe	Leu	His 95	Thr
Lys	Asn	Lys	Leu 100	Tyr	Thr	Asp	Phe	Asp 105	Glu	Ile	Arg	Gln	Glu 110	Ile	Glu
Asn	Glu	Thr 115	Glu	Arg	Ile	Ser	Gly 120	Asn	Asn	Lys	Gly	Val 125	Ser	Pro	Glu
	130			_		135			Asn		140				
145					150				Pro	155					160
_				165					11e 170		_			175	
			180					185	Ala				190		
		195					200		Glu Asp			205			
	210					215			Val		220				
225			1101		230		 1	1129	• • • •	235		V 44 1	1 275	Deu	240
Ile	Ile	Gly	Val	Val 245	Asn	Arg	Ser	Gln	Leu 250	Asp	Ile	Asn	Asn	Lys 255	Lys
			260					265	Tyr				270	_	_
		275					280		Thr			285			
	290					295			Arg		300				
305					310				Gln	315					320
				325					Ser 330 Asn					335	
			340					345	Gly				350		
		355					360					365		_	Leu
	370					375			Thr		380				
385					390				Glu	395		_			400
				405					410 Glu					415	
			420					425					430	_	
		435					440		Pro			445			
	450					455					460				Asn
465					470					475					480 Thr
		· val		485			17±C		490		nıa	тÄт	116	495	

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Lys His Pro Asp Phe Ala Asp Ala Cys Gly Leu Met Asn Asn Ile
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Glu Glu Gln Arg Arg Asn Arg Leu Ala Arg Glu Leu Pro Ser Ala Val
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Ser Arg Asp Lys Ser Ser Lys Val Pro Ser Ala Leu Ala Pro Ala Ser
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Gln Glu Pro Ser Pro Ala Ala Ser Ala Glu Ala Asp Gly Lys Leu Ile
                    550
                                        555
Gln Asp Ser Arg Arg Glu Thr Lys Asn Val Ala Ser Gly Gly Gly
                565
                                    570
Val Gly Asp Gly Val Gln Glu Pro Thr Thr Gly Asn Trp Arg Gly Met
                                585
Leu Lys Thr Ser Lys Ala Glu Glu Leu Leu Ala Glu Glu Lys Ser Lys
                            600
Pro Ile Pro Ile Met Pro Ala Ser Pro Gln Lys Gly His Ala Val Asn
                        615
Leu Leu Asp Val Pro Val Pro Val Ala Arg Lys Leu Ser Ala Arg Glu
                   630
                                        635
Gln Arg Asp Cys Glu Val Ile Glu Arg Leu Ile Lys Ser Tyr Phe Leu
                                    650
Ile Val Arg Lys Asn Ile Gln Asp Ser Val Pro Lys Ala Val Met His
            660
                                665
Phe Leu Val Asn His Val Lys Asp Thr Leu Gln Ser Glu Leu Val Gly
                            680
Gln Leu Tyr Lys Ser Ser Leu Leu Asp Asp Leu Leu Thr Glu Ser Glu
                        695
Asp Met Ala Gln Arg Arg Lys Glu Ala Ala Asp Met Leu Lys Ala Leu
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                                        715
Gln Gly Ala Ser Gln Ile Ile Ala Glu Ile Arg Glu Thr His Leu Trp
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                                    730
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Val Ala Ala Ala Val Ser Lys Thr Ala Val Ala Pro Ile Glu Arg Val
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Lys Leu Leu Gln
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      <400> 89
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                                                                     1200
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                                                                     1260
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<211> 298

<212> PRT

<213> Homo Sapiens

<400> 90

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225
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                                        235
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Glu Val Trp Thr Lys Leu Lys Ala Phe Ala Lys Ala Ser Pro Lys Cys
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                                    250
Leu Glu Asn Phe Lys Arg Gly Asn Gln Gly Lys Glu Arg Glu Lys Asn
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                                                                       120
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                                                                       180
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                                                                       240
gatgatgatt ttgaacctta cttgagtcca caggcaaggc ccaataatgc atatactgcc
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                                                                       420
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                                                                       540
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                                                                       660
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                                                                       720
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                                                                      1260
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      <211> 407
      <212> PRT
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Lys Val Gln Asn Gly Ser Val His Gln Lys Asp Gly Leu Asn Asp Asp
Asp Phe Glu Pro Tyr Leu Ser Pro Gln Ala Arg Pro Asn Asn Ala Tyr
                             40
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Thr Ala Met Ser Asp Ser Tyr Leu Pro Ser Tyr Tyr Ser Pro Ser Ile
Gly Phe Ser Tyr Ser Leu Gly Glu Ala Ala Trp Ser Thr Gly Gly Asp
                    70
                                        75
Thr Ala Met Pro Tyr Leu Thr Ser Tyr Gly Gln Leu Ser Asn Gly Glu
                                    90
Pro His Phe Leu Pro Asp Ala Met Phe Gly Gln Pro Gly Ala Leu Gly
                                105
Ser Thr Pro Phe Leu Gly Gln His Gly Phe Asn Phe Phe Pro Ser Gly
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Ile Asp Phe Ser Ala Trp Gly Asn Asn Ser Ser Gln Gly Gln Ser Thr
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Ser Ala Val Gly Ser Gly Ser Ile Thr Ser Asn Ile Val Ala Ser Asn
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Asp Ile Ala Ser Lys Pro Ala Lys Gln Gln Pro Lys Leu Lys Thr Lys
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Met Asp Ile Gly Thr Trp Asp Asn Lys Gly Pro Val Ala Lys Ala Pro
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Ser Gln Ala Leu Val Gln Asn Ile Gly Gln Pro Thr Gln Gly Ser Pro
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Gln Pro Val Gly Gln Gln Ala Asn Asn Ser Pro Pro Val Ala Gln Ala
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Ser Val Gly Gln Gln Thr Gln Pro Leu Pro Pro Pro Pro Pro Gln Pro
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Ala Gln Leu Ser Val Gln Gln Gln Ala Ala Gln Pro Thr Arg Trp Val
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                                345
Ala Pro Arg Asn Arg Gly Ser Gly Phe Gly His Asn Gly Val Asp Gly
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Asn Gly Val Gly Gln Ser Gln Ala Gly Ser Gly Ser Thr Pro Ser Glu
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<211> 2236

<212> DNA

<213> Homo Sapiens

<400> 93

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                                                                    1980
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                                                                    2040
cctctggccc agtgaatttg gtctctccca gctttggggg actccttcct tgaaccctaa
                                                                    2100
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<211> 652

<212> PRT

<213> Homo Sapiens

<400> 94

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Gln	Val 130	Gly	Asp	Glu	Ile	Val 135	Arg	Ile	Asn	Gly	Tyr 140	Ser	Ile	Ser	Ser
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		_		165	His				170					175	
_			180		Trp			185					190		
-	_	195			Ser		200					205			
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225				_	Pro 230					235					240
	_		_	245	Leu Asn				250					255	
			260		Leu			265					270		_
		275			Arg		280					285			
	290			_	Arg	295					300	_			
305					310					315					320
				325	Glu				330					335	
		_	340		Arg			345			_		350		
		355	_		Lys		360					365			
	370				Trp	375					380				
385			_		Ile 390					395					400
				405	Gln				410					415	-
			420					425					430	_	Lys
		435					440					445			Ile
	450					455					460		_		Leu
465					470					475			-		Val 480
				485					490					495	Ile
			500)				505					510		Asp
		515	;				520					525			Gln
GΤÅ	GT.	AST	rrp	тте	: Asp	ьeu	. val	val	ATa	val	Cys	Pro	Pro	ьys	Glu

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530
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Tyr Asp Asp Glu Leu Thr Phe Leu Leu Lys Ser Lys Arg Gly Asn Gln
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Ile His Ala Leu Gly Asn Ser Glu Leu Arg Pro His Leu Val Asn Thr
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Lys Pro Arg Thr Ser Leu Glu Arg Gly His Met Thr His Thr Arg Trp
            580
                               585
His Pro Trp Asp Leu Asn Leu Ser Pro Arg Asn Leu Lys Leu Pro Leu
                           600
Ala Leu Asn Gln Gly Gln Ile Arg Asn Ser Ser Gly His Phe Phe Glu
                       615
                                           620
Gly Gln Cys Gly Gly Lys Gly Ala Ala Ser Arg Leu Gly Glu Asp Leu
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Lys Asp Pro Asp Ser His Ser Phe Pro Leu Ala Gln
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aaaacnattg cagaaaacat ttagattnta tgaaatatat aatnanancc aaaanccatt
tgaanttaat ngancettae etgtenteae taaateaggg ttntetgege eacenaaggg
engeceancy cetgetgtgt tggettanta ggeetnagea tangggeagn tgeaateett
tecteetnng geggeanatg ggettetgga anaaceettn cettateeee anegeaagge
ggcccctccc ctgccctnaa aggaaacctc ntggacncag ggaatatang gccaccttga
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cctcaggccg ggagtcacct cgacactgag ggccctcggt gtgaagatga accttccacc
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           20
                               25
Arg Leu Leu Cys Trp Leu Arg Pro His Gly Cys Asn Pro Phe Leu Leu
                           40
Arg Met Gly Phe Trp Asn Pro Leu Ile Pro Ala Arg Arg Pro Leu Pro
                       55
Cys Pro Arg Lys Pro Gly Arg Glu Tyr Ala Thr Leu Lys Gly Gly Leu
                   70
                                       75
Ala Ile Glu Asp Gln Ile Pro Pro Ser Asn Leu Glu Thr Val Pro Val
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60

120

180

240

300

360

420

480

540

600

660

720

780

831

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Glu Asn Asn His Gly Phe His Glu Lys Thr Ala Ala Leu Lys Leu Glu
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                                                 125
Gly Gly Thr Gln Glu Pro Ala Pro Val Pro Ala Glu Pro Phe Asp Asn
                        135
                                            140
Thr Thr Tyr Lys Asn Leu Gln His His Asp Tyr Ser Thr Tyr Thr Phe
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                                        155
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Ser Gly Arg Glu Ser Pro Arg His
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                                                                       240
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gacagtitag caaaggcatg gaccggcaga ctgtgtctat ggcaattaat gaagtcttta
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aggatetgaa ggataagaaa ggagaeatte tettggatga aaattgetgt gtagagteet
                                                                       720
tgcctgacaa agatggaaag aaatgccttt ttctcgtaaa atgttttgat aagacttttg
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ttcatctgtt gaagctgngc agccctccac canacaaaga agccnnccag cttctnaaan
                                                                       900
aactccggna gaatcatctg gctgaacaag angaactgga gcgacaaatg aangaactcc
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Val Leu Lys Val Pro His Asp Pro Val Ala Leu Glu Glu His Phe Arg
Asp Asp Asp Glu Gly Pro Val Ser Asn Gln Gly Tyr Met Pro Tyr Leu
        35
                            40
Asn Arg Phe Ile Leu Glu Lys Val Gln Asp Asn Phe Asp Lys Ile Glu
Phe Asn Arg Met Cys Trp Thr Leu Cys Val Lys Lys Asn Leu Thr Lys
Asn Pro Leu Leu Ile Thr Glu Glu Ala Phe Lys Ile Trp Val Ile Phe
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Asn Phe Leu Ser Glu Asp Lys Tyr Pro Leu Ile Ile Val Ser Glu Ile
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                                105
Glu Tyr Leu Leu Lys Lys Leu Thr Glu Ala Met Gly Gly Gly Trp Gln
                            120
                                                125
Gln Glu Gln Phe Glu His Tyr Lys Ile Asn Phe Asp Asp Ser Lys Asn
                        135
Gly Leu Ser Ala Trp Glu Leu Ile Glu Leu Ile Gly Asn Gly Gln Phe
                    150
                                        155
Ser Lys Gly Met Asp Arg Gln Thr Val Ser Met Ala Ile Asn Glu Val
                                    170
Phe Asn Glu Leu Ile Leu Asp Val Leu Lys Gln Gly Tyr Met Met Lys
                                185
Lys Gly His Arg Arg Lys Asn Trp Thr Glu Arg Trp Phe Val Leu Lys
                            200
Pro Asn Ile Ile Ser Tyr Tyr Val Ser Glu Asp Leu Lys Asp Lys Lys
                        215
                                            220
Gly Asp Ile Leu Leu Asp Glu Asn Cys Cys Val Glu Ser Leu Pro Asp
                    230
                                        235
Lys Asp Gly Lys Lys Cys Leu Phe Leu Val Lys Cys Phe Asp Lys Thr
                245
                                    250
Phe Glu Ile Ser Ala Ser Asp Lys Lys Gln Glu Trp Ile Gln Ala Ile
                                265
                                                     270
His Ser Thr Ile His Leu Leu Lys Leu Ser Pro Pro Pro Lys Glu Ala
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gaagatgaaa cgaaaagaat ctgcatttaa gagtatgtta aaacaagctg ctcctccgat

agaattggat gctgtctggg aagatatccg tgagagattt gtaaaagagc cagcatttga

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tcataggaaa cgttcccgct ctcgatcggg gtcagattca ngatgatgat gatagccatt

caaagaaaaa aagacagcga tgagaagtct cggtctgntt canaacattc ttccantngc

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60

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180

240

300

360

420

480

540

600

660

720

780

840

900

960

<212> PRT <213> Homo Sapiens

<400> 100

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<210> 101

<211> 983

<212> DNA

<213> Homo Sapiens

<400> 101

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420

480

540

600

660

720

780

840

900

960

983

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caggetetgt gaagaaaagg gtatgettte catcagaaga teatetagag gagtttatag
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            20
                                25
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                            40
Gly Ser Leu Gly Lys Pro Leu Cys Pro Pro Glu Ile Leu Ser Glu Thr
                                            60
Leu Pro Gly Ser Val Lys Lys Arg Val Cys Phe Pro Ser Glu Asp His
                    70
Leu Glu Glu Phe Ile Ala Glu His Leu Pro Glu Ala Ser Asn Gln Ser
                                    90
Leu Leu Thr Val Ala His Ala Asp Ala Gly Thr Gln Thr Asn Gly Asp
                                105
Leu Glu Asp Leu Glu Glu His Gly Pro Gly Gln Thr Val Ser Glu Glu
                            120
Ala Thr Glu Val His Met Met Glu Gly Asp Pro Asp Thr Leu Ala Glu
                        135
                                            140
Leu Leu Ile Arg Asp Val Leu Gln Glu Leu Ser Ser Tyr Asn Gly Glu
                    150
                                        155
Glu Glu Asp Pro Glu Val Lys Thr Ser Leu Gly Val Pro Gln Arg Gly
                165
                                    170
Asp Leu Glu Asp Leu Glu Glu His Val Gly Gln Phe Ser Glu Glu Ala
            180
                                185
Thr Gly Val His Met Met Gln Val Asp Pro Ala Thr Leu Ala Lys Ser
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Asp Leu Glu Asp Leu Glu Glu His Val Pro Glu Gln Thr Val Ser Glu
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Glu Ala Thr Gly Val His
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<211> 843

<212> DNA

<213> Homo Sapiens

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cacgcccttt ctaccaagat gatagacagg atcttctcag gagcagtcac acgaggcaga
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aaagtgcaga aggaagggaa gatcagctat gccgactttg tctggttttt gatctctgag
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gaagacaaaa aaacaccgac cagcatcgag tactggttcc gctgcatgga cctggacggg
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gtcaagccga ggactgaagg gaagatcacg ctgcaggacc tgaagcgctg caagctqqcc
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tnccggccga agagtncgac atcctggtgg ccgangaaac cgtggggana nccctgggga
                                                                       660
agacgggttc naaggcgaac tcacccccnt ggancanaaa ctgantgcgc tgcgctcccc
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      <211> 197
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<212> PRT <213> Homo Sapiens

<400> 104

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                                25
Leu Ala Arg His Asn Asp His Ala Leu Ser Thr Lys Met Ile Asp Arg
                            40
Ile Phe Ser Gly Ala Val Thr Arg Gly Arg Lys Val Gln Lys Glu Gly
                        55
Lys Ile Ser Tyr Ala Asp Phe Val Trp Phe Leu Ile Ser Glu Glu Asp
                    70
Lys Lys Thr Pro Thr Ser Ile Glu Tyr Trp Phe Arg Cys Met Asp Leu
                85
                                    90
Asp Gly Asp Gly Ala Leu Ser Met Phe Glu Leu Glu Tyr Phe Tyr Glu
            100
Glu Gln Cys Arg Arg Leu Asp Ser Met Ala Ile Glu Ala Leu Pro Phe
                            120
Gln Asp Cys Leu Cys Gln Met Leu Asp Leu Val Lys Pro Arg Thr Glu
                                             140
Gly Lys Ile Thr Leu Gln Asp Leu Lys Arg Cys Lys Leu Ala Asn Val
145
                    150
                                        155
Phe Phe Asp Thr Phe Phe Asn Ile Glu Lys Leu Asp His Glu Gln Lys
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Glu Gln Ile Ser Leu Leu Arg Asp Gly Asp Ser Gly Gly Pro Glu Leu
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Ser Asp Trp Glu Lys
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<210> 105 <211> 2264 <212> DNA <213> Homo Sapiens

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cnnnnccnaa tttntanggg tttacttngn tttaaaaaac ccncccaaaa actcccccnn
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gaaccnaaaa aanaaagga ngccattttt ngnngnaaac ttttttaann nnccnnttaa
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<210> 106

<211> 381

<212> PRT

<213> Homo Sapiens

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      Val
      Val
      Pro

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      Thr
      Lys
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      Val
      Pro
      Asp
      Thr
      Ser
      Thr
      Tyr
      Gln
      Tyr
      Asp
      Glu

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      Ser
      Gly
      Tyr
      Tyr
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      Asp
      Pro
      Thr
      Thr
      Gly
      Leu
      Tyr
      Tyr
      Asp
      Pro

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      Gly
      Tyr
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      Tyr
      Asp
      Ser
      Leu
      Thr
      Gly
      Leu
      Tyr
      Tyr
      Tyr
      Tyr

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      Gly
      Glu
      Thr
      Tyr
      Val
      Pro
      Ala
      Ala
      Ala
      Glu
      Ser
      Ser
      His

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      Hy
      Tyr
      Tyr
      Yal
      Pro
      Ala
      Ala
      Ala
      Ser
      Ser
      Ser
      Hy
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Arg Gln Gln Leu Ile Pro Glu Leu Val Arg Asn Gly Asp Glu Glu Asn
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Pro Leu Lys Arg Gly Leu Val Ala Ala Tyr Ser Gly Asp Ser Asp Asn
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Glu Glu Glu Leu Val Glu Arg Leu Glu Ser Glu Glu Glu Lys Leu Ala
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Lys Asp Ala Leu Val Arg His Gln Gln Leu Ser Asp Leu His Lys Gln
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Asn Met Asp Ile Tyr Arg Arg Ser Arg Leu Ser Glu Gln Glu Leu Glu
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Glu Arg Arg Glu Lys Tyr Gly Ile Pro Glu Pro Pro Glu Pro Lys Arg
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Lys Lys Gln Phe Asp Ala Gly Thr Val Asn Tyr Glu Gln Pro Thr Lys
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                                            300
Asp Gly Ile Asp His Ser Asn Ile Gly Asn Lys Met Leu Gln Ala Met
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Gly Trp Arg Glu Gly Ser Gly Leu Gly Arg Lys Cys Gln Gly Ile Thr
                325
                                    330
Ala Pro Ile Glu Ala Gln Val Arg Leu Lys Gly Ala Gly Leu Gly Ala
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<210> 107

<211> 1367

<212> DNA

<213> Homo Sapiens

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tecetgaaga etteatetee egagagetgt ttgacacagt ecaagtgtae ateateacea
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tgctgtacta	cggcgttgtg	acactggtgt	ccatcctcca	gtactccaat	gtatactgcc	840
caacgcccaa	ggtccaggac	ctggtagatg	acaagtccct	gcaagaggca	tgtctatcct	900
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gcctgagccc	tggcactacc	gtgcgagacc	tcattggccg	ccacccccag	cagctgcagc	1020
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agaagtatcc	tgtgcgggtg	actcgggaag	agcagagcca	ccctgcccgg	ctttatacag	1140
gctgccacag	ctatgacgag	atctgctgca	agacaggcat	gagctaccat	gagctggatg	1200
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atggacacat	tgctgtgggt	agtccctcct	actaggaggc	ttgtcatact	gtctagaggt	1320
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<210> 108

<211> 413

<212> PRT

<213> Homo Sapiens

<400> 108

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275 280 285 Asp Asp Lys Ser Leu Gln Glu Ala Cys Leu Ser Tyr Val Thr Lys Gln 295 300 Gly His Lys Arg Ala Ser Leu Arg Asp Val Phe Gln Leu Tyr Cys Ser 310 315 Leu Ser Pro Gly Thr Thr Val Arg Asp Leu Ile Gly Arg His Pro Gln 325 330 Gln Leu Gln His Val Asp Glu Arg Lys Leu Ile Gln Phe Gly Leu Met 350 Lys Asn Leu Ile Arg Arg Leu Gln Lys Tyr Pro Val Arg Val Thr Arg 360 Glu Glu Gln Ser His Pro Ala Arg Leu Tyr Thr Gly Cys His Ser Tyr 375 380 Asp Glu Ile Cys Cys Lys Thr Gly Met Ser Tyr His Glu Leu Asp Glu 390 395 400 Arg Leu Glu Asn Asp Pro Asn Ile Ile Ile Cys Trp Lys 405 410

<210> 109 <211> 2113 <212> DNA <213> Homo Sapiens

<400> 109

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<210> 110

<211> 543

<212> PRT

<213> Homo Sapiens

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Lys Lys Cys Gln Gln Ala Glu Lys Ile Leu Lys Glu Gln Glu Arg Leu

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                        375
Glu Ala Ile Lys Arg Asn Pro Lys Asp Ala Lys Leu Tyr Ser Asn Arg
                    390
                                         395
Ala Ala Cys Tyr Thr Lys Leu Leu Glu Phe Gln Leu Ala Leu Lys Asp
                405
                                     410
Cys Glu Glu Cys Ile Gln Leu Glu Pro Thr Phe Ile Lys Gly Tyr Thr
                                 425
                                                     430
Arg Lys Ala Ala Ala Leu Glu Ala Met Lys Asp Tyr Thr Lys Ala Met
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Asp Val Tyr Gln Lys Ala Leu Asp Leu Asp Ser Ser Cys Lys Glu Ala
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Ala Asp Gly Tyr Gln Arg Cys Met Met Ala Gln Tyr Asn Arg His Asp
                    470
                                         475
Ser Pro Glu Asp Val Lys Arg Arg Ala Met Ala Asp Pro Glu Val Gln
                485
                                     490
Gln Ile Met Ser Asp Pro Ala Met Arg Leu Ile Leu Glu Gln Met Gln
            500
                                 505
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      <210> 111
      <211> 2765
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<212> DNA

<213> Homo Sapiens

<400> 111

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<210> 112

<211> 834

<212> PRT

<213> Homo Sapiens

<400> 112

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Pro	Ser	Ser 195	Ala	Lys	Gly	Pro	Val 200	Phe	Ser	Val	Pro	Val 205	Gly	Glu	Ile
Lys	Pro 210	Gln	Gly	Val	Tyr	Asp 215	Ile	Pro	Pro	Thr	Lys 220	Gly	Val	Tyr	Ala
225			Ser		230					235		_		_	240
			Pro	245					250					255	_
Pro	Glu	Gly	Val 260	Tyr	Asp	Ile	Pro	Pro 265	Thr	Cys	Thr	Lys	Pro 270	Ala	Gly
		275	His				280					285			
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			Gln	325					330					335	
			Glu 340					345					350		
		355	Lys				360					365		_	
	370		Ser			375					380				
385			Lys		390					395				_	400
			Leu	405					410					415	
			Leu 420					425					430		
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	450		Val			455					460				
465			Gly		470					475					480
			Lys	485					490					495	
			Ser 500					505					510	_	
		515					520					525		_	Leu
	530		Val			535					540				
545			Thr		550					555					560
			Leu -	565					570					575	
			Pro 580					585					590		
		595	Ala				600					605			
	610		Ala			615					620			_	
Trp	Met	Asp	Asp	Tyr	Asp	Tyr	Val	His	Leu	Gln	Gly	Lys	Glu	Glu	Phe

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625
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Glu Arg Gln Gln Lys Glu Leu Leu Glu Lys Glu Asn Ile Met Lys Gln
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Asn Lys Met Gln Leu Glu His His Gln Leu Ser Gln Phe Gln Leu Leu
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Glu Gln Glu Ile Thr Lys Pro Val Glu Asn Asp Ile Ser Lys Trp Lys
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Pro Ser Gln Ser Leu Pro Thr Thr Asn Ser Gly Val Ser Ala Gln Asp
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Arg Gln Leu Leu Cys Phe Tyr Tyr Asp Gln Cys Glu Thr His Phe Ile
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Ser Leu Leu Asn Ala Ile Asp Ala Leu Phe Ser Cys Val Ser Ser Ala
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Gln Pro Pro Arg Ile Phe Val Ala His Ser Lys Phe Val Ile Leu Ser
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Ala His Lys Leu Val Phe Ile Gly Asp Thr Leu Thr Arg Gln Val Thr
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Ala Gln Asp Ile Arg Asn Lys Val Met Asn Ser Ser Asn Gln Leu Cys
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Glu Gln Leu Lys Thr Ile Val Met Ala Thr Lys Met Ala Ala Leu His
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                                         795
Tyr Pro Ser Thr Thr Ala Leu Gln Glu Met Val His Gln Val Thr Asp
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Thr Phe
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<210> 113

<211> 3429

<212> DNA

<213> Homo Sapiens

<400> 113

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tecateteaa ataatgaaga aggtgtaaag ettgttegaa tgtetgeaag eeagttaqaa
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gccctctgtc ctcaggttat taatgctgca ctggctttag cagcaaaacc acagagtaaa
                                                                    1500
ctggcccaag agaacatgga tctttttaaa gaacaatggg aaaaacaagt ccqtqttctc
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                                                                    1800
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                                                                    1980
gatgactctg actttgagac agaagatttt gatgtcagaa gcaggacgag cgtccagaca
                                                                    2040
gaagacgate agetgatage tggccagagt geeegggega teatggetea getteeeeag
                                                                    2100
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                                                                    2220
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                                                                    2340
cttggccgca ccattgcaga ccattgcccc gactcggctt gcaagcagga cctgctggcc
                                                                    2400
tacctgcaac gcatcgccct ctactgccac cagctgaaca tctgcagcaa ggtcaaggcc
                                                                    2460
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                                                                    2520
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                                                                    2580
geetetacea aataeeaaaa gteacagggt atggetteee teaacettee tgetgtgtea
                                                                    2640
tggaagatga aggcaccaga gaaaaagcca ttggtgaaga gagagaaaca ggatgagaca
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                                                                    3000
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                                                                    3060
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                                                                    3120
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                                                                    3180
ttaaatgacc aaagatgacc tgtggtaagc aacctgggca tcttagaagc agtccctgga
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gaaggcatgt tcccagaaag gtctctggag ggacaaactc actcagtaaa acataatgta
                                                                    3300
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<210> 114

<211> 906

<212> PRT

<213> Homo Sapiens

<400> 114

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145	Asp				150					155					160
Ile	Leu	Lys	Leu	Arg 165	Asn	Ala	Gly	Asn	Glu 170	Gln	Asp	Leu	Gly	Ile 175	Gln
	Lys		180					185					190		
	Arg	195					200					205			
	Ala 210					215					220				
225	Gln				230					235					240
	Asp			245					250					255	
	Ala		260					265					270		_
	Gly	275					280					285			
	Ile 290					295					300				
305	Glu				310					315					320
	Ser			325					330					335	
	Asn		340					345					350		
	Asn	355					360					365			
	Lys 370					375					380				_
385	Val				390					395					400
				405					410					415	Val
	Glu		420					425					430		
	Ala	435					440					445			_
	Val 450					455					460				
465	Asn				470					475					480
	Glu			485					490					495	_
	Leu		500					505	-				510		
Ala	Val	Ser 515	Glu	Asn	His	Ile	Leu 520	Glu	Asp	Val	Asn	Lys 525	Cys	Val	Ile

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Ala Leu Gln Glu Lys Asp Val Asp Gly Leu Asp Arg Thr Ala Gly Ala
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Ile Arg Gly Arg Ala Ala Arg Val Ile His Val Val Thr Ser Glu Met
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Asp Asn Tyr Glu Pro Gly Val Tyr Thr Glu Lys Val Leu Glu Ala Thr
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                                    570
Lys Leu Leu Ser Asn Thr Val Met Pro Arg Phe Thr Glu Gln Val Glu
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Ala Ala Val Glu Ala Leu Ser Ser Asp Pro Ala Gln Pro Met Asp Glu
                           600
Asn Glu Phe Ile Asp Ala Ser Arg Leu Val Tyr Asp Gly Ile Arg Asp
                        615
Ile Arg Lys Ala Val Leu Met Ile Arg Thr Pro Glu Glu Leu Asp Asp
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                                        635
Ser Asp Phe Glu Thr Glu Asp Phe Asp Val Arg Ser Arg Thr Ser Val
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                                    650
Gln Thr Glu Asp Asp Gln Leu Ile Ala Gly Gln Ser Ala Arg Ala Ile
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Met Ala Gln Leu Pro Gln Gln Lys Ala Lys Ile Ala Glu Gln Val
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Ala Ser Phe Gln Glu Glu Lys Ser Lys Leu Asp Ala Glu Val Ser Lys
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                                            700
Trp Asp Asp Ser Gly Asn Asp Ile Ile Val Leu Ala Lys Gln Met Cys
                    710
                                        715
Met Ile Met Met Glu Met Thr Asp Phe Thr Arg Gly Lys Gly Pro Leu
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                                    730
Lys Asn Thr Ser Asp Val Ile Ser Ala Ala Lys Lys Ile Ala Glu Ala
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Gly Ser Arg Met Asp Lys Leu Gly Arg Thr Ile Ala Asp His Cys Pro
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Asp Ser Ala Cys Lys Gln Asp Leu Leu Ala Tyr Leu Gln Arg Ile Ala
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                                            780
Leu Tyr Cys His Gln Leu Asn Ile Cys Ser Lys Val Lys Ala Glu Val
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                                        795
Gln Asn Leu Gly Gly Glu Leu Val Val Ser Gly Val Asp Ser Ala Met
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                                    810
Ser Leu Ile Gln Ala Ala Lys Asn Leu Met Asn Ala Val Val Gln Thr
                                825
Val Lys Ala Ser Tyr Val Ala Ser Thr Lys Tyr Gln Lys Ser Gln Gly
                            840
Met Ala Ser Leu Asn Leu Pro Ala Val Ser Trp Lys Met Lys Ala Pro
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Glu Lys Lys Pro Leu Val Lys Arg Glu Lys Gln Asp Glu Thr Gln Thr
                   870
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<210> 115

<211> 1701

<212> DNA

<213> Homo Sapiens

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                                                                      120
cctgataaga atccccaaat gcaggagaca aactttaaag aaataagttt tgcatatgaa
                                                                      180
gtactatcaa atcctgagaa gcgtgagtta tatgacagat acggagagca aggtcttcgg
                                                                      240
gaaggcagcg gcggaggtgg gtggcatgga ttgatatttt ctctcaccgt tttttgtggg
                                                                      300
ggattgttcg gcttcatggg caatcagagt agaagtcgaa atggcagaag aagaggagag
                                                                      360
gacatgatgc atccactcaa agtatcttta gaagatctgt ataatggcaa gacaaccaaa
                                                                      420
ctacaactta gcaagaatgt gctctgtagt gcatgcagtg gccaaggcgg aaagtctgga
                                                                      480
gctgtccaaa agtgtagtgc ttgtcgaggt cgaggtgtgc gcatcatgat cagacagctg
                                                                      540
gctccaggga tggtacaaca gatgcagtct gtgtgctctg attgtaatgg tgaaggagag
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aagattettg aagteeaegt agacaaagge atgaaacatg gacagagaat tacatteact
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ggggaagcag accaggcccc agagtggaac ccggagacat tgttcttttt gctaccagga
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gaaaagaaca tggaggtatt tcagagagat gggaatgatt tgcacatgac atataaaata
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ggacttgttg aagetetatg tggattteag tteacattaa geeacettga tggacgteag
                                                                      900
attgtggtga aataccccc tggcaaagta attgaaccag ggtgtgttcg tgtagttcga
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ggtgaaggga tgccgcagta tcgtaatccc tttgaaaaag gtgggcttta cataaagttt
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caatccagct ggagtgtctt atcaatccag atgaactgag ggacatctgt tggtctatgt
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<210> 116

<211> 415

<212> PRT

<213> Homo Sapiens

<400> 116

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145
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Cys Ser Ala Cys Arg Gly Arg Gly Val Arg Ile Met Ile Arg Gln Leu
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Ala Pro Gly Met Val Gln Gln Met Gln Ser Val Cys Ser Asp Cys Asn
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Gly Glu Gly Glu Val Ile Asn Glu Lys Asp Arg Cys Lys Lys Cys Glu
                            200
Gly Lys Lys Val Ile Lys Glu Val Lys Ile Leu Glu Val His Val Asp
                        215
                                            220
Lys Gly Met Lys His Gly Gln Arg Ile Thr Phe Thr Gly Glu Ala Asp
                    230
                                        235
Gln Ala Pro Glu Trp Asn Pro Glu Thr Leu Phe Phe Leu Leu Pro Gly
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Glu Lys Asn Met Glu Val Phe Gln Arg Asp Gly Asn Asp Leu His Met
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                                265
Thr Tyr Lys Ile Gly Leu Val Glu Ala Leu Cys Gly Phe Gln Phe Thr
       275
                            280
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Leu Ser His Leu Asp Gly Arg Gln Ile Val Val Lys Tyr Pro Pro Gly
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Lys Val Ile Glu Pro Gly Cys Val Arg Val Val Arg Gly Glu Gly Met
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Pro Gln Tyr Arg Asn Pro Phe Glu Lys Gly Gly Leu Tyr Ile Lys Phe
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Asp Val Gln Phe Pro Glu Asn Asn Trp Ile Asn Pro Asp Lys Leu Ser
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Glu Leu Glu Asp Leu Leu Pro Ser Arg Pro Glu Val Pro Asn Ile Ile
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Gly Glu Thr Glu Glu Val Glu Leu Gln Glu Phe Asp Ser Thr Arg Gly
                        375
Ser Gly Gly Gln Arg Arg Glu Ala Tyr Asn Asp Ser Ser Asp Glu
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<210> 117

<211> 1821

<212> DNA

<213> Homo Sapiens

<400> 117

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agetetteet agattgacae eteetgteet tgaagaaatg ggacaetgtg acagtgttta
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cctctcagaa gttggagata ctcaggtggt ggtttttaag catgaaaagg aagatggcgc
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catttctacc atagtacttc gaggctctac agacaatctg atggatgaca tagaaagggt
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agtagacgat ggtgttaata ctttcaaagt tcttacaagg gataaacgtc ttgtacccgg
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gcttaatttt tactgtaggt gaaggctgta tttgtagtag tactcaagaa tcacctgatg
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<210> 118

<211> 548

<212> PRT

<213> Homo Sapiens

<400> 118

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Val Leu Ile Lys Thr Ala Glu Glu Leu Met Asn Phe Ser Lys Gly Glu
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Glu Asn Leu Met Asp Ala Gln Val Lys Ala Ile Ala Asp Thr Gly Ala
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Asn Val Val Thr Gly Gly Lys Val Ala Asp Met Ala Leu His Tyr
                        295
                                            300
Ala Asn Lys Tyr Asn Ile Met Leu Val Arg Leu Asn Ser Lys Trp Asp
                    310
                                        315
Leu Arg Arg Leu Cys Lys Thr Val Gly Ala Thr Ala Leu Pro Arg Leu
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Thr Pro Pro Val Leu Glu Glu Met Gly His Cys Asp Ser Val Tyr Leu
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Ser Glu Val Gly Asp Thr Gln Val Val Val Phe Lys His Glu Lys Glu
Asp Gly Ala Ile Ser Thr Ile Val Leu Arg Gly Ser Thr Asp Asn Leu
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Met Asp Asp Ile Glu Arg Val Val Asp Asp Gly Val Asn Thr Phe Lys
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Val Leu Thr Arg Asp Lys Arg Leu Val Pro Gly Gly Gly Ala Thr Glu
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Ile Glu Leu Ala Lys Gln Ile Thr Ser Tyr Gly Glu Thr Cys Pro Gly
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Leu Glu Gln Tyr Ala Ile Lys Lys Phe Ala Glu Ala Phe Glu Ala Ile
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Pro Arg Ala Leu Ala Glu Asn Ser Gly Val Lys Ala Asn Glu Val Ile
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Ser Lys Leu Tyr Ala Val His Gln Glu Gly Asn Lys Asn Val Gly Leu
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Asp Ile Glu Ala Glu Val Pro Ala Val Lys Asp Met Leu Glu Ala Gly
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Ile Leu Asp Thr Tyr Leu Gly Lys Tyr Trp Ala Ile Lys Leu Ala Thr
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Asn Ala Ala Val Thr Val Leu Arg Val Asp Gln Ile Ile Met Ala Lys
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<210> 119

<211> 1321

<212> DNA

<213> Homo Sapiens

<400> 119

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gctaaatctt gctttgcatt cagtaaagtg tcaagtgatt aagtgtgtat ttgtacccta
                                                                     1200
gatgatatga accagcagtc ttgttttggc atcatcctca tcatgttgta ttccagcttc
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<210> 120

<211> 339

<212> PRT

<213> Homo Sapiens

<400> 120

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<210> 121 <211> 2965 <212> DNA <213> Homo Sapiens

<400> 121

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	gcagttaaag					2580
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caaaaggaag	actggagaaa	tgcttacttc	tagagggaga	agactgtgcg	gcacaggaaa	2940
cagcaaacag	tggggtgatc	tgcag				2965

<210> 122

<211> 862

<212> PRT

<213> Homo Sapiens

<400> 122

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	290					205									
T.O.	Thr	Sar	Clu	GI n	T 031	295	~1 m	T7- 7	G3	a 3	300	T	-	_	_
305	1111	Der	GIU	GLII	310	Arg	GIII	vaı	GIU	315	Leu	ьуs	гйа	ràs	_
	Glu	Asp	Asp	G] 13		Gln	Δνα	T.em	λen		71 200	Tara	7 ~~	ui a	320
			- LOP	325	02	0111	A. 9	шси	330	шуз	Arg	цур	ASD	335	пуѕ
Lys	Ala	Asp	Val		Glu	Glu	Ile	Lvs		Pro	Val	Val	Cvs		T.e.11
4		-	340					345			vul	val	350	ALG	шец
Thr	Gln	Glu		Ser	Ser	Ala	Gln		Ser	Asn	Glu	Glu		His	T.e.11
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Asp	Ser	Thr	Arg	Gly	Ser	Val	His	Ser	Leu	Asp	Ala		Leu	Leu	Leu
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Pro	Ser	Gly	Asp	Pro	Phe	Ser	Lys	Ser	Asp	Asn	Asp	Met	Phe	Lys	Asp
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Gly	Leu	Arg	Arg	Ala	Gln	Ser	Thr	Asp	Ser	Leu	Gly	Thr	Ser	Gly	Ser
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Leu	Gln	Ser		Ala	Leu	Gly	Tyr	Asn	Tyr	Lys	Ala	Lys	Ser	Ala	Gly
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Asn	Leu		Glu	Ser	Asp	Phe		Pro	Leu	Val	Gly	Ala	Asp	Ser	Val
a	a 1.	435	-1	_	~ 1	_ ~	440	_				445			
ser	Glu	Asn	Pne	Asp	Thr		Ser	Leu	Gly	Ser		Gln	Met	Pro	Ser
C111	450	Mot	T 011	The	T	455	a1	G3	3		460	_			
465	Phe	Mec	neu	1111	цуs 470	Asp	GIII	GIU	Arg		ile	Lys	Ala	Met	
	Glu	Gln	Glu	Glu		Δl =	Ser	T.011	Ton	475	Cox	7707	mb	03 -	480
				485		2114	DCI	neu	490	Ser	261	val	TIII	495	GIY
Met	Glu	Ser	Ala		Val	Ser	Pro	Ser		Tvr	Ara	Len	Val		G] 11
			500	4 -				505	-	-1-		10 a	510	Der	GLU
Thr	Glu	Trp	Asn	Leu	Leu	Gln	Lys	Glu	Val	His	Asn	Ala		Asn	Lvs
		515					520					525	2		
Leu	Gly	Arg	Arg	Cys	Asp	Met	Cys	Ser	Asn	Tyr	Glu	Lys	Gln	Leu	Gln
	530					535					540				
	Ile	Gln	Ile	Gln		Ala	Glu	Thr	Arg	Asp	Gln	Val	Lys	Lys	Leu
545	_		_	_	550					555					560
Gin	Leu	Met	Leu		Gln	Ala	Asn	Asp		Leu	Glu	Lys	Thr		Lys
7 an	T ***	<i>α</i> 3 π	0 1	565	~ 1	7	Dl	-7	570	~ 3	_	_	_	575	
ASP	Lys	GIII	580	Leu	GIU	Asp	Pne		ьуs	GIn	Ser	Ser		Asp	Ser
Ser	His	Gln		Ser	Δl=	T.e.11	Ma I	585	7\ **~	717	@1 m	ח ד ת	590	a3	- 1 -
	1110	595	110	DCI	71.0	neu			Arg					GIU	TTE
Leu	Leu		Glu	Leu	Gln	Gln								Aen	₩ I
	610					615	2				620	y.D	2119	ASP	var
Gln	Glu	Gln	Met	Ala	Val	Leu	Met	Gln	Ser	Arq		Gln	Val	Ser	Glu
625					630					635					640
Glu	Leu	Val	Arg	Leu	${\tt Gln}$	Lys	Asp	Asn	Asp	Ser	Leu	Gln	Gly	Lys	
				645					650					655	
Ser	Leu	His	Val	Ser	Leu	Gln	${\tt Gln}$	Ala	Glu	Asp	Phe	Ile	Leu	Pro	Asp
_			660					665					670		
Thr	Thr		Ala	Leu	Arg	Glu		Val	Leu	Lys	Tyr	Arg	Glu	Asp	Ile
+3 -	3	675	~				680					685			
тте	Asn	val	Arg	Tnr	Ala		Asp	His	Val	Glu		Lys	Leu	Lys	Ala
۲٦,,,	690 Tlo	T ~	Dha	T 634	T	695	43	- 7 -	~ 7	2.7	700	~ 7	_	_	
705	Ile	πeμ	File	∟eu	ьуs 710	GIU	GIN	тте	GIN		Glu	GIn	Cys	Leu	-
	Asn	T,e11	Glav	Glu		Len	G3 ~	Len	C1	715	C3	7	~	T	720
		Lu	UL U	725	++1T	ueu	G111	Leu	730	TTG	GIU	ASN	cys		GLU
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Glu Ile Ala Ser Ile Ser Ser Leu Lys Ala Glu Leu Glu Arg Ile Lys
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Leu Glu Ser Leu Gln Glu Ile Lys Ile Ser Leu Glu Glu Gln Leu Lys
                        775
                                             780
Lys Glu Thr Ala Ala Lys Ala Thr Val Glu Gln Leu Met Phe Glu Glu
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                                         795
Lys Asn Lys Ala Gln Arg Leu Gln Thr Glu Leu Asp Val Ser Glu Gln
                805
                                    810
Val Gln Arg Asp Phe Val Lys Leu Ser Gln Thr Leu Gln Val Gln Leu
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                                 825
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<210> 123

<211> 544

<212> DNA

<213> Homo Sapiens

<400> 123

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<210> 124

<211> 178

<212> PRT

<213> Homo Sapiens

<400> 124

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<400> 125

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<210> 126 <211> 433

<212> PRT

<213> Homo Sapiens

<400> 126

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 Ile
 His
 Arg
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 Asp
 Ser
 Thr

 Leu
 Met
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 Val
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 Arg

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Leu Val Asp Val Leu Tyr Asn Glu Glu Lys Gln Lys Met Tyr Met Val
                            120
Met Glu Tyr Cys Val Cys Gly Met Gln Glu Met Leu Asp Ser Val Pro
                        135
Glu Lys Arg Phe Pro Val Cys Gln Ala His Gly Tyr Phe Cys Gln Leu
                    150
                                        155
Ile Asp Gly Leu Glu Tyr Leu His Ser Gln Gly Ile Val His Lys Asp
                                    170
Ile Lys Pro Gly Asn Leu Leu Thr Thr Gly Gly Thr Leu Lys Ile
            180
                                185
Ser Asp Leu Gly Val Ala Glu Ala Leu His Pro Phe Ala Ala Asp Asp
                            200
Thr Cys Arg Thr Ser Gln Gly Ser Pro Ala Phe Gln Pro Pro Glu Ile
                        215
Ala Asn Gly Leu Asp Thr Phe Ser Gly Phe Lys Val Asp Ile Trp Ser
                    230
                                        235
Ala Gly Val Thr Leu Tyr Asn Ile Thr Thr Gly Leu Tyr Pro Phe Glu
                                    250
Gly Asp Asn Ile Tyr Lys Leu Phe Glu Asn Ile Gly Lys Gly Ser Tyr
                                265
Ala Ile Pro Gly Asp Cys Gly Pro Pro Leu Ser Asp Leu Leu Lys Gly
                            280
Met Leu Glu Tyr Glu Pro Ala Lys Arg Phe Ser Ile Arg Gln Ile Arg
                        295
Gln His Ser Trp Phe Arg Lys Lys His Pro Pro Ala Glu Ala Pro Val
                    310
                                        315
Pro Ile Pro Pro Ser Pro Asp Thr Lys Asp Arg Trp Arg Ser Met Thr
                325
                                    330
Val Val Pro Tyr Leu Glu Asp Leu His Gly Ala Asp Glu Asp Glu Asp
            340
                                345
Leu Phe Asp Ile Glu Asp Asp Ile Ile Tyr Thr Gln Asp Phe Thr Val
                            360
Pro Gly Gln Val Pro Glu Glu Glu Ala Ser His Asn Gly Gln Arg Arg
                        375
Gly Leu Pro Lys Ala Val Cys Met Asn Gly Thr Glu Ala Ala Gln Leu
                                        395
Ser Thr Lys Ser Arg Ala Glu Gly Arg Ala Pro Asn Pro Ala Arg Lys
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                                    410
Ala Cys Ser Ala Ser Ser Lys Ile Arg Arg Leu Ser Ala Cys Lys Gln
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Gln
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<210> 127

<211> 1488

<212> DNA

<213> Homo Sapiens

<400> 127

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gaacttgctc gactgagaga ctcaggactc tcacagaagg aggaagagga ggacactttt 180 attgaagaac aacaactaga agaagagaag ctattggaaa gagagaggca aagattacat 240 gaggagtggt tgctaagaga gcagaaggca caagaagaat tcagaataaa gaaggaaaag 300 gaagaggcgg ctaaaaaacg gcaagaagaa caagagagaa agttaaagga acaatgggaa 360 420 gaggaagctt tgcagaagat gctggatcag gctgaaaatg agttggaaaa tggtaccaca 480 tggcaaaacc cagaaccacc cgtggatttc agagtaatgg agaaggatcg agctaattgt 540 cccttctaca gtaaaacagg agcttgcaga ttttggagata gatgttcacg taaacataat 600 ttcccaacat ccagtcctac ccttcttatt aagagcatgt ttacgacgtt tggaatggag 660 cagtgcagga gggatgacta tgaccctgac gcaagcctgg agtacagcga ggaagaaacc 720 taccaacagt tectagaett etatgaggat gtgttgeeeg agtteaagaa egtggggaaa 780 gtgattcagt tcaaggtcag ctgcaatttg gaacctcacc tgaggggcaa tgtatatgtt 840 cagtaccagt cggaagaaga atgccaagca gccctttctc tgtttaacgg acgatggtat 900 gcaggacgac agetgcagtg tgaattetge ecegtgacee ggtggaaaat ggegatttgt 960 ggtttatttg aaatacaaca atgtccaaga ggaaagcact gcaactttct tcatgtgttc 1020 agaaatccca acaatgaatt ctgggaaget aatagagaca tctacttgtc tccagatcgg 1080 actggctcct cctttgggaa gaactccgaa aggagggaga ggatgggcca ccacgacgac 1140 tactacagea ggetgegggg aaggagaaac cetagteeag accaeteeta caaaaqaaat 1200 ggggaatccg agaggaaaag tagtcgtcac agggggaaga aatctcacaa acgcacatca 1260 aagagteggg agaggeacaa tteacgaage agaggaagaa atagggaeeg cageagggae 1320 cgcagccggg gccggggcag ccggagccgg agccggagcc ggagccgcag gagccgccqc 1380 agccggagcc aaagttcctc taggtcccga agtcgtggca ggaggaggtc gggtaataqa 1440 gacagaactg ttcagagtcc caaatccaaa taaactagtt ttgttctt 1488

<210> 128

<211> 482

<212> PRT

<213> Homo Sapiens

<400> 128

Met Ala Ala Pro Glu Lys Met Thr Phe Pro Glu Lys Pro Ser His Lys 10 Lys Tyr Arg Ala Ala Leu Lys Lys Glu Lys Arg Lys Arg Arg Gln 20 25 Glu Leu Ala Arg Leu Arg Asp Ser Gly Leu Ser Gln Lys Glu Glu Glu Glu Asp Thr Phe Ile Glu Glu Gln Gln Leu Glu Glu Lys Leu Leu 55 Glu Arg Glu Arg Gln Arg Leu His Glu Glu Trp Leu Leu Arg Glu Gln 70 75 Lys Ala Glu Glu Glu Phe Arg Ile Lys Lys Glu Lys Glu Glu Ala Ala 85 90 Lys Lys Arg Gln Glu Gln Glu Arg Lys Leu Lys Glu Gln Trp Glu 105 Glu Gln Gln Arg Lys Glu Arg Glu Glu Glu Glu Gln Lys Arg Gln Glu 120 Lys Lys Glu Lys Glu Glu Ala Leu Gln Lys Met Leu Asp Gln Ala Glu 135 140 Asn Glu Leu Glu Asn Gly Thr Thr Trp Gln Asn Pro Glu Pro Pro Val 150 155 160 Asp Phe Arg Val Met Glu Lys Asp Arg Ala Asn Cys Pro Phe Tyr Ser 170 175 Lys Thr Gly Ala Cys Arg Phe Gly Asp Arg Cys Ser Arg Lys His Asn 185 Phe Pro Thr Ser Ser Pro Thr Leu Leu Ile Lys Ser Met Phe Thr Thr

		195					200					205			
Phe	Gly 210	Met	Glu	Gln	Cys	Arg 215	Arg	Asp	Asp	Tyr	Asp 220	Pro	Asp	Ala	Ser
T.011		Tur	Ser	Glu	Glu		Thr	ጥላታ	Cln	Cln.		T 011	Asp	Dha	m
225	Ora	1 Y 1	DCI	010	230	Gru	1111	TYL	GIII		PHE	Leu	Asp	PHE	-
	~		_	_			_	_		235		_	_	_	240
GIU	Asp	vai	Leu		Glu	Pne	Lys	Asn		GTA	Lys	Val	Ile	Gln	Phe
				245					250					255	
Lys	Val	Ser	Cys	Asn	Leu	Glu	Pro	His	Leu	Arg	Gly	Asn	Val	Tyr	Val
			260					265					270		
Gln	Tyr	Gln	Ser	Glu	Glu	Glu	Cys	Gln	Ala	Ala	Leu	Ser	Leu	Phe	Asn
	-	275					280					285			
Glv	Ara	Trp	Tvr	Ala	Glv	Ara	Gln	T.em	Gln	Cve	Glu		Cys	Dro	17 n T
U -1	290		- 1			295	0111	200	CIII	Cys	300	FILE	Cys	FIO	Val
mbx		m	T	Mot	71.0		C	03	T	D1			~3	~ 7	_
	Arg	пр	ьуѕ	Mec		тте	Cys	GIA	Leu		GIU	тте	Gln	GIn	_
305		_			310					315					320
Pro	Arg	Gly	Lys	His	Cys	Asn	Phe	Leu	His	Val	Phe	Arg	Asn	Pro	Asn
				325					330					335	
Asn	Glu	Phe	Trp	Glu	Ala	Asn	Arg	Asp	Ile	Tyr	Leu	Ser	Pro	Asp	Arq
			340					345		_			350	_	
Thr	Gly	Ser	Ser	Phe	Glv	Lvs	Asn	Ser	Glu	Ara	Ara	Glu	Arg	Met	Glv
	-	355			-	-	360			3	5	365	5		
His	His	Asn	Asp	Tyr	ጥኒፖ	Ser		T.611	Ara	Glar	7, 200		Asn	Dro	C02
11110	370	ı.cp		- 7 -	- y -	375	**** 9	LCu	AL 9	Gry	380	Arg	ASII	PIO	ser
Dwo		TT d a	C 0 m	Mr	T		70	61	a 3	~			_	_	_
	Asp	nis	ser	ıyı		Arg	ASI	GIA	GIU		GIu	Arg	Lys	ser	
385		_		_	390		_			395					400
Arg	His	Arg	GIA		Lys	Ser	His	Lys	Arg	Thr	Ser	Lys	Ser	Arg	Glu
				405					410					415	
Arg	His	Asn	Ser	Arg	Ser	Arg	Gly	Arg	Asn	Arg	Asp	Arg	Ser	Arg	Asp
			420					425					430	_	_
Arg	Ser	Arg	Gly	Arg	Gly	Ser	Arq	Ser	Arg	Ser	Arq	Ser	Arg	Ser	Ara
		435	_	_	_		440		-			445			3
Ara	Ser	Ara	Ara	Ser	Ara	Ser	Gln	Ser	Ser	Ser	Ara		Arg	Ser	Δνα
3	450	د	3		5	455			~~1	201	460	501	9	JCI	131 Y
Glar		Δνα	Δνα	Sar	Glar		71 ~~~	λ ~~	7. 200	πh		~ 1	Ser	Desc	T
465	A.y	n.y	ar 9	DET		UDII	Arg	Asp	Arg		val	GIN	ser	Pro	-
	.				470					475					480
ser	Lys														

<210> 129

<211> 1663

<212> DNA

<213> Homo Sapiens

<400> 129

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aatgtggcaa agcctttagt aatagctcaa atctcaccaa acacaqqaqa acacacactq
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gggagaaacc ttacgtgtgc accaagtgtg ggaaagcttt cagccacagc tcaaacctca
                                                                      780
ccctccacta cagaacacac ttggtggacc ggccctatga ctgtaagtgt ggaaaaqctt
                                                                      840
ttgggcagag ctcagacctt cttaaacatc agagaatgca cacagaagag gcgccatatc
                                                                      900
agtgcaaaga ttgtggcaag gctttcagcg ggaaaggcag cctcattcgt cactatcgga
                                                                      960
tecacactgg ggagaageet tateagtgta acgaatgtgg gaagagette agteageatg
                                                                      1020
cgggcctcag ctcccaccag agactccaca ccggagagaa gccatataag tgtaaggagt
                                                                      1080
gtgggaaagc cttcaaccac agctccaact tcaataaaca ccacagaatc cacaccgggg
                                                                      1140
aaaagcccta ctggtgtcat cactgtggaa agaccttctg tagcaagtcc aatctttcca
                                                                     1200
aacatcagcg agtccacact ggagagggag aagcaccgta actttcaagc gctcctgttg
                                                                     1260
ttgtcgttgt tttaaacttt agaatctgaa aaccagaaag aagtcttgtc attgcagcag
                                                                     1320
categattcc ggtgatagag tttgtatcac tcaacatcag gggatgcctg aggagtgcqa
                                                                      1380
gctccacage aacatggcag gcaggaggtc ctcagaaggt gtcaggaggt tccacactcq
                                                                     1440
ccagttcact ggagcagagt cccttcgcca cacttagggt cccagtaagc catgccagca
                                                                     1500
ttaccttttg cgtagttaaa cagacgtgta tccagtctag ttaaggaaga aacattaaqa
                                                                     1560
ttgtttaatt tttaacatat attcaagaat tttaatttgt aaagaattga gccacattga
                                                                      1620
acacaattga atgagattca gaataaactt ataacatctt aaa
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<210> 130

<211> 412

<212> PRT

<213> Homo Sapiens

<400> 130

Ala Leu Ser Gln Leu Arg Val Leu Cys Cys Glu Trp Leu Arg Pro Glu 10 Ile His Thr Lys Glu Gln Ile Leu Glu Leu Val Leu Glu Gln Phe 25 Leu Thr Ile Leu Pro Gln Glu Leu Gln Ala Trp Val Gln Glu His Cys 40 Pro Glu Ser Ala Glu Glu Ala Val Thr Leu Leu Glu Asp Leu Glu Arg 55 Glu Leu Asp Glu Pro Gly His Gln Val Ser Thr Pro Pro Asn Glu Gln 70 75 Lys Pro Val Trp Glu Lys Ile Ser Ser Ser Gly Thr Ala Lys Glu Ser 85 90 Pro Ser Ser Met Gln Pro Gln Pro Leu Glu Thr Ser His Lys Tyr Glu 110 Ser Trp Gly Pro Leu Tyr Ile Gln Glu Ser Gly Glu Glu Gln Glu Phe 120 Ala Gln Asp Pro Arg Lys Val Arg Asp Cys Arg Leu Ser Thr Gln His 135 140 Glu Glu Ser Ala Asp Glu Gln Lys Gly Ser Glu Ala Glu Gly Leu Lys 150 Gly Asp Ile Ile Ser Val Ile Ile Ala Asn Lys Pro Glu Ala Ser Leu 165 170 Glu Arg Gln Cys Val Asn Leu Glu Asn Glu Lys Gly Thr Lys Pro Pro 185 190 Leu Gln Glu Ala Gly Ser Lys Lys Gly Arg Glu Ser Val Pro Thr Lys 200 Pro Thr Pro Gly Glu Arg Arg Tyr Ile Cys Ala Glu Cys Gly Lys Ala 215 220 Phe Ser Asn Ser Ser Asn Leu Thr Lys His Arg Arg Thr His Thr Gly Glu Lys Pro Tyr Val Cys Thr Lys Cys Gly Lys Ala Phe Ser His Ser

```
245
                                    250
Ser Asn Leu Thr Leu His Tyr Arg Thr His Leu Val Asp Arg Pro Tyr
                                265
Asp Cys Lys Cys Gly Lys Ala Phe Gly Gln Ser Ser Asp Leu Leu Lys
                            280
His Gln Arg Met His Thr Glu Glu Ala Pro Tyr Gln Cys Lys Asp Cys
                        295
Gly Lys Ala Phe Ser Gly Lys Gly Ser Leu Ile Arg His Tyr Arg Ile
                    310
                                        315
His Thr Gly Glu Lys Pro Tyr Gln Cys Asn Glu Cys Gly Lys Ser Phe
                325
                                    330
Ser Gln His Ala Gly Leu Ser Ser His Gln Arg Leu His Thr Gly Glu
Lys Pro Tyr Lys Cys Lys Glu Cys Gly Lys Ala Phe Asn His Ser Ser
                            360
Asn Phe Asn Lys His His Arg Ile His Thr Gly Glu Lys Pro Tyr Trp
                        375
                                            380
Cys His His Cys Gly Lys Thr Phe Cys Ser Lys Ser Asn Leu Ser Lys
                    390
                                        395
His Gln Arg Val His Thr Gly Glu Gly Glu Ala Pro
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<210> 131

<211> 724

<212> DNA

<213> Homo Sapiens

<400> 131

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<210> 132

<211> 218

<212> PRT

<213> Homo Sapiens

<400> 132

PCT/US98/14679 WO 99/04265

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Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys Gln Ile Glu
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                                        75
Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu Asp Glu Lys
                                    90
Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu Leu Glu Asp
            100
                                105
Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn Leu Ile Ile
                            120
Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln Lys His Asp
                        135
                                             140
Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg Glu Glu Ser
                    150
                                         155
Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala Val Val Ile
                                    170
Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly Asp Leu Lys
            180
                                185
Arg Arg Val His Glu Ala Gln Glu Lys Asn Glu Lys Leu Thr Lys Glu
        195
                            200
                                                 205
Leu Glu Glu Ile Ser Pro Pro Ser Gln Lys
    210
      <210> 133
      <211> 719
      <212> DNA
      <213> Homo Sapiens
      <400> 133
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tggtggaggg tttgcagaaa caacccagga gaccaaggcg gtgactgtcc atgttcacgg
                                                                       120
ccaggaagtc ctgtcagagg agacggtgca tttaggagcg gagcctgagt cacctaatga
                                                                       180
gctgcaggat cctgtgcaaa gctcgacccc cgagcagtct cctgaggaaa ccacacagag
                                                                       240
cccagatctg ggggcaccgg cagagcagcg tccacaccag gaagaggagc tccagaccct
                                                                       300
gcaggagage gaggtcccag tgcccgagga cccagacctt cctgcagaga ggagctctgg
                                                                       360
agactcagag atggttgctc ttcttactgc tctgtcacag ggactggtaa cgttcaaqqa
                                                                       420
tgtggccgta tgcttttccc aggaccagtg gagtgatctg gacccaacac agaaaqaqtt
                                                                       480
ctatggagaa tatgtcttgg aagaagactg tggaattgtt gtctctctgt catttccaat
                                                                       540
ccccagacct gatgagatct cccaggttag agaggaagag cccttgggtc ccagatatcc
                                                                       600
aagageetna ggagaeteaa gageeagaaa teetgagttt taeetacaca ggagatagga
                                                                       660
gtnaagatga aggaaaatgt ctggagccag gaagaatctg agtttggagg atataccca
                                                                       719
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      <211> 217
      <212> PRT
      <213> Homo Sapiens
      <400> 134
Arg Thr Thr Glu Leu Gly Ala Gly Pro Thr Ala Arg Lys Trp Arg Gly
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Gly Ser Asp Ala Gly Gly Gly Phe Ala Glu Thr Thr Gln Glu Thr Lys
            20
Ala Val Thr Val His Val His Gly Gln Glu Val Leu Ser Glu Glu Thr
                             40
Val His Leu Gly Ala Glu Pro Glu Ser Pro Asn Glu Leu Gln Asp Pro
```

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Val Gln Ser Ser Thr Pro Glu Gln Ser Pro Glu Glu Thr Thr Gln Ser
                    70
                                        75
Pro Asp Leu Gly Ala Pro Ala Glu Gln Arg Pro His Gln Glu Glu Glu
                                    90
Leu Gln Thr Leu Gln Glu Ser Glu Val Pro Val Pro Glu Asp Pro Asp
            100
                                105
Leu Pro Ala Glu Arg Ser Ser Gly Asp Ser Glu Met Val Ala Leu Leu
                            120
                                                125
Thr Ala Leu Ser Gln Gly Leu Val Thr Phe Lys Asp Val Ala Val Cys
                                            140
Phe Ser Gln Asp Gln Trp Ser Asp Leu Asp Pro Thr Gln Lys Glu Phe
                    150
Tyr Gly Glu Tyr Val Leu Glu Glu Asp Cys Gly Ile Val Val Ser Leu
                165
                                    170
Ser Phe Pro Ile Pro Arg Pro Asp Glu Ile Ser Gln Val Arg Glu Glu
                                185
Glu Pro Leu Gly Pro Arg Tyr Pro Arg Ala Gly Asp Ser Arg Ala Arg
                            200
Asn Pro Glu Phe Tyr Leu His Arg Arg
    210
                        215
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      <212> DNA
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                                                                       120
egeaegtget ggaaeeggat gaggaeetge agegeetgea getetegege eageagetee
                                                                       180
aggtcacggg agacgccagc gagagcgccg aggacatett ettecggegg gccaaggagg
                                                                       240
gcatgggcca ggacgaggcg cagttcagcg tggagatgcc actcaccggc aagqcctacc
                                                                       300
tgtgggccga caagtaccgg ccacgcaagc cgcgcttctt caaccgcgtg cacacgggct
                                                                       360
tegagtggaa caagtacaac cagacgcact acgaetttga caacccaccg cecaagateg
                                                                       420
tgcagggata caagttcaac atcttctacc ccgacctcat cgacaagcgc tccacgcccg
                                                                       480
agtacttcct ggaggcctgc gccgacaaca aggatttcgc catcctgcgc ttcacgcggg
                                                                       540
gccgcctacg aggacatcgc tttcaagatc gtcaaccgcg agtgggaata ctngcaccgc
                                                                       600
caeggettee getgecagtt tgccaaegge attttccane tgngctttca cttcaagege
                                                                       660
tneegetate ggeggtgaeg geeetgggga aeggeaggee aggagggeeg agggeeacae
                                                                       720
gggtgccaca gcccaggtcg gagtggccca gccggcaggc ttgtttttca gcatccgacg
                                                                       780
ggaacatctc caacagaagc aaaacggaaa gtgcctcccg gacccccaga qqqccaccca
                                                                       840
acctcaccag tcaccagece cagaccacce acagececte ecagacacce egecteatet
                                                                       900
ggaaatagtt ccgtttgttt ctctaaaaaag acttgtaggt gggaaaaaaa atcttttqqt
                                                                       960
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ataaaaa
                                                                      1027
      <210> 136
      <211> 299
      <212> PRT
      <213> Homo Sapiens
      <400> 136
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Ser Leu Asp Asp Tyr Asp Ala Gly Arg Tyr Ser Pro Arg Leu Leu Thr

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Ala His Glu Leu Pro Leu Asp Ala His Val Leu Glu Pro Asp Glu Asp
                             40
Leu Gln Arg Leu Gln Leu Ser Arg Gln Gln Leu Gln Val Thr Gly Asp
Ala Ser Glu Ser Ala Glu Asp Ile Phe Phe Arg Arg Ala Lys Glu Gly
                                         75
Met Gly Gln Asp Glu Ala Gln Phe Ser Val Glu Met Pro Leu Thr Gly
                85
                                     90
Lys Ala Tyr Leu Trp Ala Asp Lys Tyr Arg Pro Arg Lys Pro Arg Phe
                                 105
Phe Asn Arg Val His Thr Gly Phe Glu Trp Asn Lys Tyr Asn Gln Thr
                            120
His Tyr Asp Phe Asp Asn Pro Pro Pro Lys Ile Val Gln Gly Tyr Lys
    130
                        135
Phe Asn Ile Phe Tyr Pro Asp Leu Ile Asp Lys Arg Ser Thr Pro Glu
                    150
                                         155
Tyr Phe Leu Glu Ala Cys Ala Asp Asn Lys Asp Phe Ala Ile Leu Arg
                                    170
Phe Thr Arg Gly Arg Leu Arg Gly His Arg Phe Gln Asp Arg Gln Pro
            180
                                185
Arg Val Gly Ile Leu Ala Pro Pro Arg Leu Pro Leu Pro Val Cys Gln
                            200
Arg His Phe Pro Leu Ser Leu Gln Ala Leu Pro Leu Ser Ala Val Thr
                        215
Ala Leu Gly Asn Gly Arg Pro Gly Gly Pro Arg Ala Thr Arg Val Pro
                    230
                                         235
Gln Pro Arg Ser Glu Trp Pro Ser Arg Gln Ala Cys Phe Ser Ala Ser
                245
                                    250
Asp Gly Asn Ile Ser Asn Arg Ser Lys Thr Glu Ser Ala Ser Arg Thr
                                265
Pro Arg Gly Pro Pro Asn Leu Thr Ser His Gln Pro Gln Thr Thr His
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                            280
                                                 285
Ser Pro Ser Gln Thr Pro Arg Leu Ile Trp Lys
    290
                        295
      <210> 137
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<211> 766

<212> DNA

<213> Homo Sapiens

<400> 137

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                                                                       120
tggaacacca atttggtgca caaggggacc tcaccacgga atgtgctact gcaaacaacc
                                                                       180
ccacagccat cacgcctgat gagtacttca atgaagagtt tgatctgaaa gacagggaca
                                                                       240
ttggaaggcc gaaagagctg acgattagaa cacagaagtt taaagcaatg ttgtggatgt
                                                                       300
gtgaagagtt teceetetet etggtggage aggteattee cateattgae etaatggete
                                                                       360
gaacgagtgc tcattttgca agactgagag atttcatcaa attggaattc ccacctggat
                                                                       420
ttcctgtcaa aatagcttcc cacatcacaa actttgaggt tgatcaatct gtgtttgaaa
                                                                       480
ttcccgaatc ttactatgtt caagacaatg gcagaaatgt gcatttgcaa gatgaagatt
                                                                       540
acgagataat gcagtttgcc atccagcaaa gtctgctgga gtccagcagg agccaggaac
                                                                      600
tttcaggacc agcttcgaat ggagggatca gccagacaaa cacctatgac gcccagtatg
                                                                      660
agagggccat neaggagage ettetaceag cacagaaage etgtgeeece agegeeetg
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                                                                      766
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<210> 138 <211> 243 <212> PRT <213> Homo Sapiens

<400> 138

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<210> 139 <211> 3060 <212> DNA <213> Homo Sapiens

<400> 139

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<210> 140

<211> 872

<212> PRT

<213> Homo Sapiens

<400> 140

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Pro	Glu	Ala 115	Arg	Pro	Asp	Gly	Glu 120	Gly	Ser	Pro	Gly	Lys 125	Ala	Arg	Pro
	130					135					140			Asp	
145					150					155				Glu	160
				165					170					Pro 175	
			180					185					190	Val	
		195					200					205		Ala	
	210					215					220			Val	-
225					230					235				Ser	240
				245					250					Phe 255	
			260					265					270	Trp	
		275					280					285		Met	
	290					295					300			Ser	
305					310					315				Arg	320
				325					330					Asn 335	
			340					345					350	Ser	_
		355					360					365		Ser	
	370					375					380				Pro
385					390					395					Ser 400
				405					410					Pro 415	
			420					425					430		Thr
		435					440					445		Arg	_
	450					455					460				Pro
465					470					475					Gly 480
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                               505
Tyr Leu Ser His Leu Glu Ala Leu Leu Pro Met Lys Pro Leu Lys
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Thr Ile Phe Phe Lys Val Pro Glu Leu Tyr Glu Ile His Lys Glu Phe
                   550
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Tyr Asp Gly Leu Phe Pro Arg Val Gln Gln Trp Ser His Gln Gln Arg
                                   570
Val Gly Asp Leu Phe Gln Lys Leu Ala Ser Gln Leu Gly Val Tyr Arg
           580
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                           600
Cys Gln Ala Asn Ala Gln Phe Ala Glu Ile Ser Glu Asn Leu Arg Ala
                       615
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Arg Ser Asn Lys Asp Ala Lys Asp Pro Thr Thr Lys Asn Ser Leu Glu
                   630
                                       635
Thr Leu Leu Tyr Lys Pro Val Asp Arg Val Thr Arg Ser Thr Leu Val
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                                   650
Leu His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro
                               665
           660
Leu Leu Gln Asp Ala Leu Arg Ile Ser Gln Asn Phe Leu Ser Ser Ile
                           680
Asn Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly
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Glu His Arg Gln Leu Leu Lys Asp Ser Phe Met Val Glu Leu Val Glu
                    710
                                       715
Gly Ala Arg Lys Leu Arg His Val Phe Leu Phe Thr Glu Leu Leu Leu
                                   730
Cys Thr Lys Leu Lys Lys Gln Ser Gly Gly Lys Thr Gln Gln Tyr Asp
                               745
Cys Lys Trp Tyr Ile Pro Leu Thr Asp Leu Ser Phe Gln Met Val Asp
                         760
Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val Pro Asp Glu Glu Leu
                       775
                                           780
Asp Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys Ser Asp Ile Gln Arq
                   790
Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys
                805
                                   810
Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Met Ser Pro Ser Met
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Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile
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<211> 691

<212> DNA

<213> Homo Sapiens

<400> 141

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                                                                       120
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                                                                       420
cattacttca tecetgtcat etgatggggt ceteactgtg aatggaccaa ggaaacaggt
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ccccaaqaaa taqatqccct ttcttqaatt qcatttttta aaacaaqaaa qtttccccac
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cagtgaatga aagtcttgtg actagtgctg aagcttatta atgctaaggg caggcccaaa
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<210> 142

<211> 175

<212> PRT

<213> Homo Sapiens

<400> 142

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<210> 143

<211> 1300

<212> DNA

<213> Homo Sapiens

<400> 143

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170

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tcaaagatca tgaagagcaa gataaagtca gacctaaagc caaaaggaaa gaagaaccaa
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                                                                      540
cacccaaatt tgtgcagcta aagcctggag aaaagcctgt tcaagtggat caaacaaaqa
                                                                      600
aagaggcaga acctatacca gaaactgtaa aacctgagga gaaggagacc cccnnagaat
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gtacaaccag accgggagtg ctaaaggccc ccctgaaaaa cggatgagac ttcagtgagt
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<210> 144

<211> 233

<212> PRT

<213> Homo Sapiens

<400> 144

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Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala
                        55
Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro
                    70
Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile
                85
                                     90
Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr
            100
                                105
Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys
Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu
                        135
Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser
                    150
                                         155
Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg
                                     170
Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys Pro
                                                     190
Val Gln Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu Thr
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                                                 205
Val Lys Pro Glu Glu Lys Glu Thr Pro Glu Cys Thr Thr Arg Pro Gly
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Val Leu Lys Ala Pro Leu Lys Asn Gly
225
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<210> 145 <211> 1528

<212> DNA <213> Homo Sapiens

<400> 145

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<210> 146

<211> 449

<212> PRT

<213> Homo Sapiens

<400> 146

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Leu 145	Glu	Ser	Pro	Asp	Phe 150	Gln	Pro	Asn	Ile	Ala 155	Lys	Lys	Tyr	Ile	Asp 160
Gln	Lys	Phe	Val	Leu 165	Gln	Leu	Leu	Glu	Leu 170	Phe	Asp	Ser	Glu	Asp 175	Pro
Arg	Glu	Arg	Asp 180	Phe	Leu	Lys	Thr	Thr 185	Leu	His	Arg	Ile [°]	Tyr 190	Gly	Lys
Phe	Leu	Gly 195	Leu	Arg	Ala	Tyr	Ile 200	Arg	Lys	Gln	Ile	Asn 205	Asn	Ile	Phe
Tyr	Arg 210	Phe	Ile	Tyr	Glu	Thr 215	Glu	His	His	Asn	Gly 220	Ile	Ala	Glu	Leu
Leu 225	Glu	Ile	Leu	Gly	Ser 230	Ile	Ile	Asn	Gly	Phe 235	Ala	Leu	Pro	Leu	Lys 240
Glu	Glu	His	Lys	Ile 245	Phe	Leu	Leu	Lys	Val 250	Leu	Leu	Pro	Leu	His 255	Lys
Val	Lys	Ser	Leu 260	Ser	Val	Tyr	His	Pro 265	Gln	Leu	Ala	Tyr	Cys 270	Val	Val
		275	Glu		_		280					285			
Leu	Leu 290	Lys	Tyr	Trp	Pro	Lys 295	Thr	His	Ser	Pro	300	Glu	Val	Met	Phe
305			Leu		310			_		315					320
			Met	325					330				_	335	
			Phe 340					345					350		
		355	Met				360	_				365			
	370		Pro			375				_	380		_		_
Thr 385	Ile	His	Gly	Leu	Ile 390	Tyr	Asn	Ala	Leu	Lys 395	Leu	Phe	Met	Glu	Met 400
Asn	Gln	Lys	Leu	Phe 405	Asp	Asp	Cys	Thr	Gln 410	Gln	Phe	Lys	Ala	Glu 415	Lys
Leu	Lys	Glu	Lys 420	Leu	Lys	Met	Lys	Glu 425	Arg	Glu	Glu	Ala	Trp 430	Val	Lys
Ile	Glu	Asn 435	Leu	Ala	Lys	Ala	Asn 440	Pro	Gln	Val	Leu	Lys 445	Lys	Arg	Ile
Thr															

Thr

<210> 147

<211> 1580

<212> DNA

<213> Homo Sapiens

<400> 147

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<212> PRT

<213> Homo Sapiens

<400> 148

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Trp Val Arg Gln Pro Val Gln Val Pro Val Thr Leu Val Arg Asn Asp
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Gly Pro Arg Pro His Cys Ser Val Ala Gly Ala Ile Leu Pro Ala Asn
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Ser Ser Gln Val Pro Pro Asn Glu Ser Asn Thr Asn Ser Glu Gly Ser
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600

660

720

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<211> 297

<212> PRT

<213> Homo Sapiens

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<211> 1953 <212> DNA <213> Homo Sapiens

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<210> 152 <211> 572 <212> PRT <213> Homo Sapiens

<400> 152

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 Ser
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 Lys

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 Arg
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 Thr

 Follow
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 Arg
 Ile
 Thr

 Follow
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 Arg
 Ile
 PCT/US98/14679

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Ala Ile Ser Glu Glu Asn Thr Lys Glu Glu Lys Pro Asp Ser Lys Lys
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Gln Glu Met Gly Asp Glu Asn Ala Glu Ile Thr Glu Glu Met Met Asp
            100
                                105
Gln Ala Asn Asp Lys Lys Val Ala Ala Ile Glu Ala Leu Asn Asp Gly
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Glu Leu Gln Lys Ala Ile Asp Leu Phe Thr Asp Ala Ile Lys Leu Asn
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Pro Arg Leu Ala Ile Leu Tyr Ala Lys Arg Ala Ser Val Phe Val Lys
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Leu Gln Lys Pro Asn Ala Ala Ile Arg Asp Cys Asp Arg Ala Ile Glu
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Ile Asn Pro Asp Ser Ala Gln Pro Tyr Lys Trp Arg Gly Lys Ala His
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Arg Leu Leu Gly His Trp Glu Glu Ala Ala His Asp Leu Ala Leu Ala
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Cys Lys Leu Asp Tyr Asp Glu Asp Ala Ser Ala Met Leu Lys Glu Val
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Gln Pro Arg Ala Gln Lys Ile Ala Glu His Arg Arg Lys Tyr Glu Arg
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                                        235
Lys Arg Glu Glu Arg Glu Ile Lys Glu Arg Ile Glu Arg Val Lys
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                                    250
Ala Arg Glu Glu His Glu Arg Ala Gln Arg Glu Glu Glu Ala Arg Arg
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Gln Ser Gly Ala Gln Tyr Gly Ser Phe Pro Gly Gly Phe Pro Gly Gly
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Met Pro Gly Asn Phe Pro Gly Gly Met Pro Gly Met Gly Gly Met
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Pro Gly Met Ala Gly Met Pro Gly Leu Asn Glu Ile Leu Ser Asp Pro
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                                        315
Glu Val Leu Ala Ala Met Gln Asp Pro Glu Val Met Val Ala Phe Gln
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                                    330
Asp Val Ala Gln Asn Pro Ala Asn Met Ser Lys Tyr Gln Ser Asn Pro
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<211> 1323

<212> DNA

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                                                                       540
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gtaatacatt cataagacaa gtgaaagaag agcatggcag acacacagat gcaactgtga
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(213) Home Bapiens

<400> 156

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Asn Pro Asp Arg Ser Phe Asp Val Glu Ser Val Lys Lys Glu Ile Gln
Arg Gly Arg Lys Leu Lys Cys Lys Phe Cys His Lys Arg Gly Ala Thr
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Val Gly Cys Asp Leu Lys Asn Cys Asn Lys Asn Tyr His Phe Phe Cys
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Ala Lys Lys Asp Asp Ala Val Pro Gln Ser Asp Gly Val Arg Gly Ile
            1.00
                                105
Tyr Lys Leu Leu Cys Gln Gln His Ala Gln Phe Pro Ile Ile Ala Gln
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Ser Ala Lys Phe Ser Gly Val Lys Arg Lys Arg Gly Arg Lys Lys Pro
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Leu Ser Gly Asn His Val Gln Pro Pro Glu Thr Met Lys Cys Asn Thr
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Val Lys Val Pro Phe Leu Lys Lys Cys Lys Gly Ser Arg Thr Ser
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<210> 157

<211> 4065

<212> DNA

<213> Homo Sapiens

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<213> Homo Sapiens

<400> 158

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	1090)				1095	5				1100)		Val	
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				1125	5				1130)				Arg 1135	5
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<211> 732

<212> PRT

<213> Homo Sapiens

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tcaggaaagc agagagcttg aagaaatgtc tctctgtcat ggaagccaaa gtgaaggctc
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agactgetee aaacaaggat gtgeagaggg agategetga eettggagag geeetggeea
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<210> 171 <211> 1004

<212> PRT

<213> Homo Sapiens

<400> 171

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Ser	Ile	Asp 275	Thr	Gly	Met	Gly	Leu 280	Glu	Arg	Leu	Val	Ser 285	Val	Leu	Gln
Asn	Lys 290	Met	Ser	Asn	Tyr	Asp 295	Thr	Asp	Leu	Phe	Val 300	Pro	Tyr	Phe	Glu
Ala 305	Ile	Gln	Lys	Gly	Thr 310	Gly	Ala	Arg	Pro	Tyr 315	Thr	Gly.	Lys	Val	Gly 320
Ala	Glu	Asp	Ala	Asp 325	Gly	Ile	Asp	Met	Ala 330	Tyr	Arg	Val	Leu	Ala 335	Asp
His	Ala	Arg	Thr 340	Ile	Thr	Val	Ala	Leu 345		Asp	Gly	Gly	Arg 350		Asp
Asn	Thr	Gly 355	Arg	Gly	Tyr	Val	Leu 360		Arg	Ile	Leu	Arg 365		Ala	Val
Arg	Tyr 370	Ala	His	Glu	Lys	Leu 375	Asn	Ala	Ser	Arg	Gly 380	Phe	Phe	Ala	Thr
Leu 385		Asp	Val	Val	Val 390		Ser	Leu	Gly	Asp 395		Phe	Pro	Glu	Leu 400
	Lys	Asp	Pro	Asp		Val	Lys	Asp	Ile 410		Asn	Glu	Glu	Glu 415	
Gln	Phe	Leu	Lys 420		Leu	Ser	Arg	Gly 425		Arg	Ile	Leu	Asp		Lys
Ile	Gln	Ser 435	Leu	Gly	Asp	Ser	Lys 440		Ile	Pro	Gly	Asp		Ala	Trp
Leu	Leu 450		Asp	Thr	Tyr	Gly 455		Pro	Val	Asp	Leu 460		Gly	Leu	Ile
Ala		Glu	Lys	Gly	Leu		Val	Asp	Met	Asp		Phe	Glu	Glu	Glu
465					470					475					480
Arg	Lys	Leu	Ala	Gln 485	Leu	Lys	Ser	Gln	Gly 490	Lys	Gly	Ala	Gly	Gly 495	Glu
Asp	Leu	Ile	Met 500	Leu	Asp	Ile	Tyr	Ala 505	Ile	Glu	Glu	Leu	Arg 510	Ala	Arg
Gly	Leu	Glu 515	Val	Thr	Asp	Asp	Ser 520	Pro	Lys	Tyr	Asn	Tyr 525	His	Leu	Asp
Ser	Ser 530	Gly	Ser	Tyr	Val	Phe 535	Glu	Asn	Thr	Val	Ala 540	Thr	Val	Met	Ala
Leu	Arg	Arg	Glu	Lys	Met	Phe	Val	Glu	Glu	Val	Ser	Thr	Gly	Gln	Glu
545	~.7			_	550	_	_,	_		555					560
			Val	565					570					575	_
			Asp 580					585				-	590		
Asp	Lys	Thr 595	Glu	Phe	Thr	Val	Lys 600	Asn	Ala	Gln	Val	Arg 605	Gly	Gly	Tyr
Val	Leu 610	His	Ile	Gly	Thr	Ile 615	Tyr	Gly	Asp	Leu	Lys 620	Val	Gly	Asp	Gln
Val 625	Trp	Leu	Phe	Ile	Asp 630	Glu	Pro	Arg	Arg		Pro	Ile	Met	Ser	
	Thr	Δla	Thr	Hic		T. 2 11	Agn	Dhe	Δ] =	635	λνα	Sor	1757	T.a.r	640
				645					650					655	_
			Gln 660	-				665			_	_	670	_	
Asp	Phe	Thr 675	Ala	Lys	Gly	Ala	Met 680	Ser	Thr	Gln	Gln	Ile 685		Lys	Ala
Glu	Glu 690	Ile	Ala	Asn	Glu	Met 695		Glu	Ala	Ala	Lys 700		Val	Tyr	Thr
Gln		Cys	Pro	Leu	Ala			Lys	Ala	Ile			Leu	Arg	Ala

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710
705
                                        715
Val Phe Asp Glu Thr Tyr Pro Asp Pro Val Arg Val Val Ser Ile Gly
                                    730
Val Pro Val Ser Glu Leu Leu Asp Asp Pro Ser Gly Pro Ala Gly Ser
                                745
Leu Thr Ser Val Glu Phe Cys Gly Gly Thr His Leu Arg Asn Ser Ser
                            760
His Ala Gly Ala Phe Val Ile Val Thr Glu Glu Ala Ile Ala Lys Gly
                        775
Ile Arg Arg Ile Val Ala Val Thr Gly Ala Glu Ala Gln Lys Ala Leu
                    790
                                        795
Arg Lys Ala Glu Ser Leu Lys Lys Cys Leu Ser Val Met Glu Ala Lys
                805
                                    810
Val Lys Ala Gln Thr Ala Pro Asn Lys Asp Val Gln Arg Glu Ile Ala
                                825
Asp Leu Gly Glu Ala Leu Ala Thr Ala Val Ile Pro Gln Trp Gln Lys
                            840
Asp Glu Leu Arg Glu Thr Leu Lys Ser Leu Lys Lys Val Met Asp Asp
                        855
                                            860
Leu Asp Arg Ala Ser Lys Ala Asp Val Gln Lys Arg Val Leu Glu Lys
                    870
Thr Lys Gln Phe Ile Asp Ser Asn Pro Asn Gln Pro Leu Val Ile Leu
                885
                                    890
Glu Met Glu Ser Gly Ala Ser Ala Lys Ala Leu Asn Glu Ala Leu Lys
                                905
Leu Phe Lys Met His Ser Pro Gln Thr Ser Ala Met Leu Phe Thr Val
        915
                            920
Asp Asn Glu Ala Gly Lys Ile Thr Cys Leu Cys Gln Val Pro Gln Asn
                        935
                                            940
Ala Ala Asn Arg Gly Leu Lys Ala Ser Glu Trp Val Gln Gln Val Ser
                    950
                                        955
Gly Leu Met Asp Gly Lys Gly Gly Lys Asp Val Ser Ala Gln Ala
                965
                                    970
Thr Gly Lys Asn Val Gly Cys Leu Gln Glu Ala Leu Gln Leu Ala Thr
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Ser Phe Ala Gln Leu Arg Leu Gly Asp Val Lys Asn
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<211> 659

<212> DNA

<213> Homo Sapiens

<400> 172

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ggaaaactca gattccaatg acaaaggaag tggtgatcag tctgcagcac agcqcaqaaq
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tcagatggac cgattggatc gagaagaagc tttctatcaa tttgtaaata acctgagtga
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agaagattat aggcttatga gagataacaa tttgctaggc accccaggtg aaagtactga
                                                                      360
ggaagagttg ctgagacgac tacagcaaat taaagaaggc ccaccaccgc aaaactcaga
                                                                      420
tgaaaataga ggaggagact cttcagatga tgtgtctaat ggtgactcta taatagactg
                                                                      480
gcttaactct gtcagacaaa ctggaaatac aacaagaagt gggcaaagag qaaaccaatc
                                                                      540
ttggagagca gtgagtcgga ctaatccaaa cagtgggtga tttcagattc agtttagaga
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taaatgttaa cccgtaataa tgggagccaa aattcagaga atgaaaatga gccatctgc
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Gln Leu Leu Ile Gly Gly Gly Leu Glu Ser Gly Gly Gln Gly Gly Ala
Glu Gln Pro Arg Arg Arg Pro Asn Gln Pro Ser Arg Ile Leu Thr
                            40
Leu Lys Pro Ser Ile Phe His Leu Phe Ile Asn Met Glu Asn Ser Asp
                        55
Ser Asn Asp Lys Gly Ser Gly Asp Gln Ser Ala Ala Gln Arg Arg Ser
                    70
Gln Met Asp Arg Leu Asp Arg Glu Glu Ala Phe Tyr Gln Phe Val Asn
                85
                                    90
Asn Leu Ser Glu Glu Asp Tyr Arg Leu Met Arg Asp Asn Asn Leu Leu
                                105
Gly Thr Pro Gly Glu Ser Thr Glu Glu Glu Leu Leu Arg Arg Leu Gln
                            120
                                                125
Gln Ile Lys Glu Gly Pro Pro Pro Gln Asn Ser Asp Glu Asn Arg Gly
                        135
                                            140
Gly Asp Ser Ser Asp Asp Val Ser Asn Gly Asp Ser Ile Ile Asp Trp
145
                    150
                                        155
Leu Asn Ser Val Arg Gln Thr Gly Asn Thr Thr Arg Ser Gly Gln Arg
                165
                                    170
Gly Asn Gln Ser Trp Arg Ala Val Ser Arg Thr Asn Pro Asn Ser Gly
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                                                    190
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                                                                       120
caaccccaaa tetgecacag agcagteagg aactggtate egateagaga gtgagacaga
                                                                       180
gtccgaggcc tcagaaatta ctattcctcc cagcaccccg gcagttccac aggctcccgt
                                                                       240
ccagggggag gactacggca aaggtgtcat cttctacctc agggacaaag tggtcgtggg
                                                                       300
gattgtgcta tggaacatct ttaaccgaat gccaatagca aggaagatca ttaaggacgg
                                                                       360
tgagcagcat gaagatctca atgaagtagc caaactattc aacattcatg aagactgaag
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<213> Homo Sapiens

<400> 175

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540

600

610

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Tyr Trp His Gln Ser Met Phe Trp Ser Asp Leu Gly Pro Asp Val Gly
                                    10
Tyr Glu Ala Ile Gly Leu Val Asp Ser Ser Leu Pro Thr Val Gly Val
            20
Phe Ala Lys Ala Thr Ala Gln Asp Asn Pro Lys Ser Ala Thr Glu Gln
                            40
Ser Gly Thr Gly Ile Arg Ser Glu Ser Glu Thr Glu Ser Glu Ala Ser
Glu Ile Thr Ile Pro Pro Ser Thr Pro Ala Val Pro Gln Ala Pro Val
                    70
Gln Gly Glu Asp Tyr Gly Lys Gly Val Ile Phe Tyr Leu Arg Asp Lys
                                    90
Val Val Gly Ile Val Leu Trp Asn Ile Phe Asn Arg Met Pro Ile
                                105
                                                    110
Ala Arg Lys Ile Ile Lys Asp Gly Glu Gln His Glu Asp Leu Asn Glu
        115
                            120
Val Ala Lys Leu Phe Asn Ile His Glu Asp
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                                                                       120
gtccgcgcca tggccatcta caagcagtca cagcacatga cggaggttgt gaggcgctgc
                                                                       180
ecceaceatg agegetgete agatagegat ggtetggece etecteagea tettateega
                                                                       240
gtggaaggaa atttgcgtgt ggagtatttg gatgacagaa acacttttcg acatagtgtg
                                                                       300
gtggtgccct atgagccgcc tgaggttggc tctgactgta ccaccatcca ctacaactac
                                                                       360
atgtgtaaca gttcctgcat gggcggcatg aaccggaggc ccatcctcac catcatcaca
                                                                       420
ctggaagact ccagtggtaa tctactggga cggaacagct ttgaggtgcg tgtttgtgcc.
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tgtcctggga gagaccggcg cacagaggaa gagaatctcc gcaagaaagg ggagcctcac
                                                                       540
cacgaagetg ceeecaggga geactaageg ageaetgeec aacaacacea ageteetete
                                                                       600
cccagccaaa gaagaaanca ctggatngag aatatttcac cccttcanat tcgttgggcg
                                                                       660
tgagcgcttc cganaatgtt ccgaagagct gnaagaaggc cttgggaact caaaggatgc
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ccaaggettg ggaaaggage caangggggg gaancaangg geteaactne aagceaacet
                                                                       780
gaaagttcca aaaaangggt ccagt
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                                                                       120
caggtttgca ggcaggccgt catgagtgcc ggtggaaggc tccgagggcg tgggcagggg
                                                                       180
ctcgggcggg gccacacact tgtggagcta gaaatantgg ggcaggtcct tctctatcac
                                                                       240
caggggctcc tccatgggtc cgtagcgctt caccacgcag ccgttcttgt cgatgaggaa
                                                                       300
ctgtgganan acggtgtcca aactgtgggg ccacccctgc aaggggctga ggctgccctt
                                                                       360
cetgteeget geceatetgg gecaeggetg tggceagggg aaactggtee cetaececee
                                                                       420
acagececet tacetttggt gaagtteeac ttgatggeac tggaaaanaa geacatggae
                                                                       480
gtgagcgtcc ccaggcagcc ccccacagtc cccaaagctt gtcctgtctc caaggaggcc
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tecteacega ggaagggetg etgettatee egeceaagea getgeaacae cageageage
                                                                     240
300
aacccagtgg ccccgctgtc gccagcctcg agccgccggt caagctcaag gaactgcact
                                                                     360
tetecaacat gaagacegtg gaetgtgtgg agegeaaggg caagtacatg tactteactg
                                                                     420
tggtgatggc agagggcaag gagatcgact ttcggtgccc gcaagaccag ggctggaacq
                                                                     480
ccgagatcac gctgcagatg gtgcagtaca agaatcgtca ggccatcctg gcggtcaaat
                                                                     540
ccacgeggca gaagcagcag cacetggtee ageancagee eceetegcag eegcageege
                                                                     600
agecgeaget ecaagececa acceeageet teagecteaa geengeaace ecaagececa
                                                                     660
attcacaaac cccaagecet caagececaa cccaaagece tcangececa ngcaagntee
                                                                     720
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                                                                     780
acccaanaac nct
                                                                     793
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ctccaagatt aggaattact acggattagg tttttgaaaa taaagtttcc tttttggaaa
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                                                                     240
aaatcaaaat acattaaaat aaaattacag tacatcatcg ctcctagaaa attcaccata
                                                                     300
caagacgatc ctttcaaagg ttcataaata aaagtcttct tgactcgaaa tcgtttcctg
                                                                     360
catcgtgatg aaaagtatgc agaaaactaa gaagaatcgc aagttttcag tagggtgatg
                                                                     420
tccaaactac ttgatctggt gcggggcgga gagactgttt tgcttttgat ccaagtgaag
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                                                                     600
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tggggtgcca antnaaggat gaaaatgtgg atnttngnat nttgattccg gatacggggt
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ccctcatggc ctcttctccg acttctatct gtgtgtgtgg gcaggtgcca gctggggtgg
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gagttctgca gtgtgacctg tgtcaggact ggttccatgg gcagtgtgtg tcagtgccc
                                                                     240
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atotoctoac ototocaaag occagtotoa ottoatotoc actgotageo tggtgggaat
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gggacacaaa atteetgtgt eeaetgtgta tgegeteaeg aeggeeaege etagagacaa
                                                                     360
tectageett getggttgee etgeagagge tgeeegtgeg getgeetgag ggtgaggeee
                                                                     420
ttcagtgtct cacagagagg gccattggct ggcaagaccg tgccagaaag gctctggcct
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ctgaagatgt gactgetetg ttgegacage tggetgaget tegecaacag etacaggeca
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accagteetg agaacatgge tecaggaaag ggetetgace tggagetaen gteeteactg
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                                                                     120
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                                                                     240
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                                                                     300
gatttgtttg tccctattca gactagaatg aaactggttt aggaaatcac tcctgtatgc
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tagcaggaat gttgctggca agacacttct gagcatcgqq qtqtqqactt tacqaaccaa
                                                                     420
ccttttaaca gtaactctag gagagagat atcaaaaatt ggcagtgaaa aattatagat
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acaataacaa ccacaaatgg acctttggtg ccactgtcac aactgttgct catcagagta
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ggagaattgt ancaaaggca ttaaagaagg gacaagcaag ctgaagagcc tgaatccttg
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gggttgtaag cenattttgg gntteettte aagaaaaggg etgttggneg gtggaanggg
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tcanggaaca ntatttcacg ggtcngc
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tgctcaatga aataaaagag gatacaaaca aatggaagaa cattccatgc tcatgggtag
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gaagaatcaa tatcgtgaaa atggccatac tgcccaaggt aatgtataga ttcaatgcca
                                                                     240
tececateaa getaceaatg aetttettea cagaattgga aaaaaetaet caaaagttea
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tatggaacca aaaaagagcc cacattgcca agtcaatcct aagccaaaag aacaaagctg
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ggtactggta ccaaaacaga gatataaatc aatgcaacag aacagagccc tcagaaataa
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                                                                     660
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480

540

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atctcgaaag agcagatnaa gggcctnaan ctatcgaaca gattcacaaa ganggctaaa
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attgaaanaa caagaatagc caaagggaag gnccaacaac tcatggacca anggagaaat
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                                                                       360
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                                                                       420
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tgagaattgt gggtgaactt gagcagatgg tttctgagga cgtcccgctg gaccaccgcg
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ttcacgeceg catcattggt geeegeggca aagecatteg caaaatcatg gacgaattea
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ggctcccaga gaatgtggag gaagccatcg accacatcct caatctggag gaggaatacg
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acctgggacc gccagcaacc aatnaaaaaa ggcnctgacn ttaaccaagc tcngagggaa
                                                                       840
tttcccancc tttgggggcc caaggtggct cccaaagaac cctccccntt nggggcccc
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<213> Homo Sapiens

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ggagtengtt atentaacae gaatgeecan gacettggtt taatgttaaa cantqqaqea
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ngtectgane gggeaeggee angeetggag ganeggeege acacacanee angegenagg
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ctccctgcgg gacctcngga agggggaana gcgtcaacaa tttacggngg gtccaaccqc
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tgggtcaaat tgagacaaac cantgtgtgg ttgggttcgg gtcancangc tqqananqqt
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tengttentt ttgateanta nentttgggg ecceaaggga nggtentggg anecacetga
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nccccaaagc tgggaaattc ctcaaagctg cncatgtcaa gagccttcnc antgctgctq
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geggteeaag gtgegteeeg caccacaaag cetetggaag gngeentgge etetteetgt
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gennaagaca ggaatnacag ggtcagtctg cccaacaacc ccancatccc ggcccgccct
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ggctcaaacc ctgcaacctt gcctgccttc cqqqaancac aatttcccac ccttqtnccc
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ctgaaancen cetggnetgg ggeenteaaa ggeegttgga netteeanag gneneeceea
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ggggntccca angggcccac aa
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tgcatttcta tcgtaaccgg gcgcggggga gcgcagatcg gcgcccagca atcacagaaq
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aactctgata tgatggaaaa cagcaaggaa gagggaacta gctcttcaga aaaatccaag
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tottcaggat cgtcacgatc aaagaggaaa ccttcaattq taacaaaqta tqtaqaatca
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gatgatgaaa aacctttgga tgatgaaact gtaaatgaag atgcgtctaa tgaaaattca
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gtgctgaatg aagacaaaga tgattttaaa ggggcctgaa tttagaagca gaagttaaaa
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tgaaaactga naatctcaaa aaacgccgga gaanatgggc ttcatgggga ttqtqanqcc
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tgcactggcn tggtggacaa caaggtcaat caatttcaaa aaggttccat ttatagacaa
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cccttcaatg caaggtcnta tttgtta
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gattggcaaa atccagtatg tgaagacagc actaaatttt cagtcacagg cttaattttc
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tgttcatcgc tgcttccctc acctatagaa ttctgatcat catcttctat atcagaagaa
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gatgaggatg taatgtcagc ttgcttcctt ttagtgcttg ttcttaggga gtttctcttt
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                                                                       420
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ttctctttga acttaaattt cttctttccc tcaattcgag tcttttcagt caccttatca
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608

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                                                                       120
ttatgagaaa agtgaagttt tatgatgaaa acacaaggca gtggtggatg ccggataccg
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gaggagetaa cateccaget etgaatgage tgetgtetgt gtggaacatg gggtteageg
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atggcctgta tgaaggggag ttcaccctgg ccaaccatga catgtattat gcgtcaqqqt
                                                                       300
gcagcatege gaagttteca gaagatggeg tegtgataac acagaettte aaggaecaag
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gattggaggt tttaaagcag gaaacagcag ttgttgaaaa cgtccccatt ttgggacttt
                                                                       420
atcagattcc agctgagggt ggaggccgga ttgtactgta tggggactcc aattgcttgg
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atgacagtca ccgacagaag gactgctttt ggcttctgga tgccctcctc cagtacacat
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cgtatggggt gacaccgcct agcctcagtc actctgggaa ccgccagcgc cctcccantt
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ggagcaaget cagteactec agagaggatg gaaggaaace ateteategg tactecaagg
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ttctggangg ccatttggga aaaccaaaac ctcgggctcn acaaccctgt ccangcctgt
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nctgggccaa gccaanagcc tttaaaccan aacggngccc aattaaccct ttggaaaaca
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cagatttgtg catgtttcct tcaaatctca gtctgtactg tcattaaaaa gatcatggaa
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gecaacacag cteggnteac ceaecanege egteegtnaa aggggetete tggggeeteac
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gaanctggcg gggngcttca accetgggct tecteeggct tteggeetgg neetgggeet
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420

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cccctgctac ccaaaatggt aatttggttc aaagtgttaa gtcaacctcc cttqataqca
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tetttggnan gttettttga etecaagagg aagaangtnt ngtteatgtn antangeaan
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antgtngnat naccgncngn c
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<211> 818

<212> DNA

<213> Homo Sapiens

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<210> 207 <211> 910 <212> DNA

<213> Homo Sapiens

<400> 207

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taaaacntgg ncttgaaaga aaatttcaca actagttnag aaacttgtta ccaaatggta
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aaggaaaaag tcaactggga aaaattcaag ggngttaana aaaanttggt ttacctgggg
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cccaageett ttgngaaaaa aaaaneeeet tatgaaanee cengggeeca aaaanaettt
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<212> DNA <213> Homo Sapiens

<400> 210

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<210> 211

<211> 972

<212> DNA

<213> Homo Sapiens

<400> 211

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<211> 817

<212> DNA

<213> Homo Sapiens

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agaaaggntc accttgacca accagtttta tgcaacgaan tggctgggaa tngagaacca
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720

765

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240

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240

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480

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420

480

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180

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780

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<212> DNA

<213> Homo Sapiens

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WO 99/04265

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<210> 557 <211> 328

<212> PRT

<213> Homo Sapiens

<400> 557

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Glu Gly Gly Val Asp Ser Pro Ile Gly Lys Val Val Val Ser Ala Val
                    150
Tyr Glu Arg Gly Ala Ala Glu Arg His Gly Gly Ile Val Lys Gly Asp
                165
                                     170
Glu Ile Met Ala Ile Asn Gly Lys Ile Val Thr Asp Tyr Thr Leu Ala
                                185
                                                     190
Glu Ala Asp Ala Ala Leu Gln Lys Ala Trp Asn Gln Gly Gly Asp Trp
        195
                            200
Ile Asp Leu Val Val Ala Val Cys Pro Pro Lys Glu Tyr Asp Asp Glu
                        215
Leu Thr Phe Leu Leu Lys Ser Lys Arg Gly Asn Gln Ile His Ala Leu
225
                                         235
Gly Asn Ser Glu Leu Arg Pro His Leu Val Asn Thr Lys Pro Arg Thr
                245
                                     250
Ser Leu Glu Arg Gly His Met Thr His Thr Arg Trp His Pro Trp Asp
                                 265
Leu Asn Leu Ser Pro Arg Asn Leu Lys Leu Pro Leu Ala Leu Asn Gln
                            280
Gly Gln Ile Arg Asn Ser Ser Gly His Phe Phe Glu Gly Gln Cys Gly
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                                             300
Gly Lys Gly Ala Ala Ser Arg Leu Gly Glu Asp Leu Lys Asp Pro Asp
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Ser His Ser Phe Pro Leu Ala Gln
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<210> 558 <211> 2289 <212> DNA

<213> Homo Sapiens

<400> 558

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gtgtggactc ccccattggg aaggtggtcg tttctgctgt gtatgagcgg ggagctgctg
                                                                     1620
ageggeatgg tggeattgtg aaaggggaeg agateatgge aateaaegge aagattgtga
                                                                     1680
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                                                                     1740
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                                                                     1800
tettgetgaa gteeaaaagg ggaaaccaaa tteacgegtt aggaaacagt gageteegge
                                                                     1860
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gatggcatcc ttgggacctg aatctatcac ccaggaatct caaactccct ttggccctga
                                                                     1980
accagggcca gataaggaac agctcgggcc acttttttga aggccaatgt ggaggaaagg
                                                                     2040
gagcagccag ccgtttggga gaagatctca aggatccaga ctctcattcc tttcctctgg
                                                                     2100
cccagtgaat ttggtctctc ccagctttgg gggactcctt ccttqaaccc taataaqacc
                                                                     2160
ccactggagt ctctctct ccatccctct cctctgccct ctgctctaat tgctgccagg
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<210> 559

<211> 481

<212> PRT

<213> Homo Sapiens

<400> 559

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260
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Glu Ala Val Asn Val Leu Lys Asn Ser Arg Ser Leu Thr Ile Ser Ile
        275
                            280
Val Ala Ala Gly Arg Glu Leu Phe Met Thr Asp Arg Glu Arg Leu
                        295
                                            300
Ala Glu Ala Arg Gln Arg Glu Leu Gln Arg Gln Glu Leu Leu Met Gln
                    310
                                        315
Lys Arg Leu Ala Met Glu Ser Asn Lys Ile Leu Gln Glu Gln Glu Glu
                325
                                    330
Met Glu Arg Gln Arg Lys Glu Ile Ala Gln Lys Ala Ala Glu Glu
                                345
Asn Glu Arg Tyr Arg Lys Glu Met Glu Gln Ile Val Glu Glu Glu Glu
                            360
Lys Phe Lys Lys Gln Trp Glu Glu Asp Trp Gly Ser Lys Glu Gln Leu
                        375
                                            380
Leu Leu Pro Lys Thr Ile Thr Ala Glu Val His Pro Val Pro Leu Arq
                    390
                                        395
Lys Pro Lys Tyr Asp Gln Gly Val Glu Pro Glu Leu Glu Pro Ala Asp
                405
                                    410
Asp Leu Asp Gly Gly Thr Glu Glu Gln Gly Glu Gln Pro Gln Glu Met
            420
                                425
                                                     430
Leu Lys Arg Met Val Val Tyr Gln Asp Ser Ile Gln Asp Lys Ile Ser
        435
                            440
Gly Asn Met Arg Lys Ala Leu Thr Pro Thr Leu Cys Ser Pro Gln Ser
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Arg Ser Trp Gly Arg Met Ser Gly Ser Tyr Ala Ser Arg Arg Asp
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Pro
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<210> 560 <211> 2409 <212> DNA

<213> Homo Sapiens

<400> 560

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                                                                     1260
accatcactg ctgaggtaca cccagtaccc cttcgcaagc caaagtatga tcagggagtg
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                                                                     1800
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                                                                     1980
cccacctcgt gaacacaaag cctcggacca gccttgagag aggccacatg acacacca
                                                                     2040
gatggcatcc ttgggacctg aatctatcac ccaggaatct caaactccct ttggccctga
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accagggcca gataaggaac agctcgggcc acttttttga aggccaatgt ggaggaaagg
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                                                                     2280
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<210> 561

<211> 521

<212> PRT

<213> Homo Sapiens

<400> 561

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Glu Lys Lys Val Phe Ile Ser Leu Val Gly Ser Arg Gly Leu Gly Cys
                        215
                                            220
Ser Ile Ser Ser Gly Pro Ile Gln Lys Pro Gly Ile Phe Ile Ser His
                    230
                                        235
Val Lys Pro Gly Ser Leu Ser Ala Glu Val Gly Leu Glu Ile Gly Asp
                245
                                    250
Gln Ile Val Glu Val Asn Gly Val Asp Phe Ser Asn Leu Asp His Lys
            260
                                265
Glu Ala Val Asn Val Leu Lys Asn Ser Arg Ser Leu Thr Ile Ser Ile
        275
                            280
Val Ala Ala Gly Arg Glu Leu Phe Met Thr Asp Arg Glu Arg Leu
                        295
                                            300
Ala Glu Ala Arg Gln Arg Glu Leu Gln Arg Gln Glu Leu Leu Met Gln
305
                    310
                                        315
Lys Arg Leu Ala Met Glu Ser Asn Lys Ile Leu Gln Glu Gln Glu
                325
                                    330
Met Glu Arg Gln Arg Arg Lys Glu Ile Ala Gln Lys Ala Ala Glu Glu
                                345
Asn Glu Arg Tyr Arg Lys Glu Met Glu Gln Ile Val Glu Glu Glu
                            360
                                                365
Lys Phe Lys Lys Gln Trp Glu Glu Asp Trp Gly Ser Lys Glu Gln Leu
                        375
                                            380
Leu Leu Pro Lys Thr Ile Thr Ala Glu Val His Pro Val Pro Leu Arg
                    390
                                        395
Lys Pro Lys Tyr Asp Gln Gly Val Glu Pro Glu Leu Glu Pro Ala Asp
                405
                                    410
Asp Leu Asp Gly Gly Thr Glu Glu Gln Gly Glu Gln Thr Phe Cys Pro
                                425
Ser Pro Gln Pro Pro Arg Gly Pro Gly Val Ser Thr Ile Ser Lys Pro
                            440
Val Met Val His Gln Glu Pro Asn Phe Ile Tyr Arg Pro Ala Val Lys
                        455
                                            460
Ser Glu Val Leu Pro Gln Glu Met Leu Lys Arg Met Val Val Tyr Gln
                    470
                                        475
Asp Ser Ile Gln Asp Lys Ile Ser Gly Asn Met Arg Lys Ala Leu Thr
                485
                                    490
Pro Thr Leu Cys Ser Pro Gln Ser Arg Ser Trp Gly Arg Met Ser Gly
            500
                                505
Ser Tyr Ala Ser Arg Arg Arg Asp Pro
      <210> 562
      <211> 1445
      <212> DNA
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<213> Homo Sapiens

<400> 562

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                                                                       120
gaaagctgaa tgaggttcag agcttctctg aagctcaaac agaaatggtg aggacgcttq
                                                                       180
agcggaagtt agaagcaaaa atgatcaagg aggaaagcga ctaccacgac ctggagtcgg
                                                                       240
tggttcagca ggtggagcag aacctggagc tgatgaccaa acgggctgta aaggcagaaa
                                                                       300
accacgtcgt gaaactaaaa caggaaatca gtttgctcca ggcgcaggtc tccaacttcc
                                                                       360
agcgagagaa tgaagccctg cggtgcggcc agggtgccag cctgaccgtg gtgaagcaga
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                                                                       600
gcatgaagct ccgtgtatac cctgaggtca ccaccgctcg atctaaatgt gcagttgtgt
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ccagtcccat cccagaacat cagttgtaag ataagtacaa ttggttgtcc ttgatttcat
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aagtagaaca aacactaaat gtgcctctga gatggccacc ccgggcaggg acctgtgcct
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teegeegatg eteagggete cetetggete eegggteact ettgtggeee eagtgggtgg
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tecetgeagt catggeetga gtgegeaggg geeacegegt ggetgetget gteeteetee
                                                                     1140
ggggaccacg ggggaacaag gtcacacctt ccgtgctgtg aagctgtcca gatgtgcctc
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tttggctggg ggttttggtg gacgtttcaa gtggcatttt gtacaatgca ggttagaatt
                                                                     1260
caggaatttc aagtatgtgc ccgggtntgt caggtcccag ttgcctttnt qacqqcccc
                                                                     1320
ctcagaggga cggcgatgag cactaaatgc ttttttgant attttcctat agatttttt
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tcacc
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<210> 563

<211> 192

<212> PRT

<213> Homo Sapiens

<400> 563

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<210> 564

<211> 1226

<212> DNA

<213> Homo Sapiens

<400> 564

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                                                                       180
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                                                                       300
actgccggcg cgccctggag ctggacgggc agtctgtgaa ggcgcacttc ttcctggggc
                                                                       360
agtgccagct ggagatggag agctatgatg aggccatcgc caatctgcag cgagcttaca
                                                                       420
gcctggccaa ggagcagcgg ctgaacttcg gggacgacat ccccagcgct cttcgaatcq
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cgaagaagaa gcgctggaac agcattgagg agcggcgcat ccaccaggag agcgagctgc
                                                                       540
actectacet etecaggete attgcegegg agegtgagag ggagetggaa gagtgecage
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gaaaccacga gggtgatgag gacgacagcc acgtccgggc ccagcaggcc tgcattgagg
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ccaagcacga caagtacatg gcggacatgg acgagctttt ttctcaggtg gatgagaaga
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ggaagaageg agacateeee gactacetgt gtggcaagat cagetttgag etgatgeggg
                                                                       780
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ccaacttggc tatgaaggag gttattgacg cattcatctc tgagaatggc tgggtggagg
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cccggcccct aaacatagtt tatgtttttg gccaccccga ccgcttcccc caagttctgc
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tgttggactc tggactgttt cccctctcag catcgctttt gctgggccgt gattgtcccc
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<212> PRT

<213> Homo Sapiens

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Ile Glu Glu His Leu Gln Arg Val Gly His Phe Asp Pro Val Thr Gly
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Ser Pro Leu Thr Gln Glu Gln Phe Ile Pro Asn Leu Ala Met Lys Glu
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<213> Homo Sapiens

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<212> PRT

<213> Homo Sapiens

<400> 569

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165
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Pro Arg Glu Ile Lys Arg Leu Lys Lys Glu Lys Pro Glu Glu Glu Val
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Lys Lys Leu Lys Pro Lys Gly Thr Lys Asn Phe Ser Leu Leu Ser Phe
                    70
                                        75
Gly Glu Glu Ala Glu Glu Glu Glu Glu Val Asn Arg Val Ser Gln
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	FIO	1112	115	Ser	Ser	vaı	PIO	120	vaı	GIU	Ser	GIU		GIY	Asp	Ala
	Δla	Agn		77 o 7	Asp	λαn	C1 11		7.00	C7.,	C02	77.	125	TT	7	G3
,-	пια	130	Бец	vai	ASP	дая	135	GIU	ASP	GIU	ser		Gru	HIS	Asp	Giu
	Tur		Aen	Clv	Asp	Gl 11		7 02	Ton	Mot	71 ~~~	140	71 200	71 a	71.7	7
	145	**C	Hap	Gry	нар	150	цуѕ	ASII	ьеи	Mec	155	GIU	Arg	тте	Ara	_
		T.e.11	Lare	Lara	Asp		Sar	λ 1 ¬	λan	17-1		Com	71 7 ~	<i>α</i> 1	a1	160
•	шуз	neu	шуз	цур	165	TILL	Set	MIA	ASII	170	ьуѕ	ser	Ата	GIA		GIÀ
	Glu	17::1	Glu	Larg		Car	77-1	602	71 200		a1	~1	*	7	175	~3
*	GIU	Val	GIU	180	Lys	261	val	Set	185	ser	GIU	GIU	Leu	_	ьys	Giu
	Δla	Δνα	Gln		Tare	7 ~~	Glu	Ton		ת דת	ח ד ת	C1	a1	190	T	**- 3
	лта	nr 9	195	neu	Lys	Arg	GIU	200	ьeu	ALG	Ата	GIU		ьys	ьуs	va⊥
_	Glu	Aen		71 2	Larc	Gl n	77-		Tira	7 ~~~	Com	a1	205	~1	61	
_	GIU	210	на	ALG	Lys	GIII		Gru	гуу	Arg	ser		Gru	GIU	GIU	Ala
	Dro		7. an	C111	7.7.	1707	215	a 1	m	7	7	220	~	~7	_	_
		PIO	ASP	GIY	Ala		Aid	GIU	TAT	Arg		GIU	ьуs	GIn	ьуs	=
	225	77.	T	70	T	230	~ 1	a	.	•	235	1	_	_		240
	GIU	Ald	Leu	Arg	Lys	GIN	GII	ser	ьуѕ		GTĀ	Thr	Ser	Arg		Asp
	~1 m	mb as	T	77-	245	T	7	41.	D1	250	_	_	_		255	
	GIII	THE	neu		Leu	Leu	Asn	GIN		гàг	ser	Lys	Leu		Gln	Ala
	т1.	77.	a1	260	D	a 1	1	7	265	.	~ 3		~ 3	270		
	TTE	MIA	275	1111	Pro	GIU	ASII		тте	Pro	GIU	Thr		Vai	Glu	Asp
	Λαn	C111		m-see	7.// a. b.	Com	TT	280	T	a 1	D1	~ 3	285	_	_	_
	АЗР	290	Сту	пр	Met	DEI		val	ьеи	GTII	Pne		Asp	ràs	Ser	Arg
	Two		Tara	7 ~~	77.	0	295 Mat	~1	70	0	3	300	-1	~ 7		_
	305	Vai	ьуѕ	Asp	Ala		Met	GIN	Asp	ser		Thr	Phe	Glu	Ile	-
		Dro	7 ~~	7 an	Drea	310	7. ~~~	T	7	7	315	G 3	~ 7	_	_	320
	мар	FIO	Arg	ASII	Pro	vai	ASII	ьуѕ	Arg		Arg	GIU	GIU	ser	_	Lys
	T.em	Mot	Ara	Glu	325 Lys	Tara	C'111	70.00	7. ~~~	330	T 0	D	77-7	3	335	~ 7
	шсц	FICE	Arg	340	цуъ	пуs	GIU	Arg	345	TTE	Leu	Pro	vai		Giu	Gly
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•	cga	gcct	age o	acta	tcaa	ag ci	tate	aata	c ad	cato	caas	ct.c:	acta(aad : -~⊃ c	aacat	tcgacg
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	acga	acga	cac o	cttc	acct	ga o	cca	cacc	a cti	tcao	adac 2-33	aga (aacae:	aas (CCŒŒ ∍~∋⊋;	gcagcg gcgagc
	cct	gggg	egg (cggc	cact	ce to	gcaci	tttc	t cc	aata	aaaa	acc	caac	acc :	taat taat	ggcacc
*	ggg	ccago	gcc (cagg	cgga	tg ci	tqcad	acct	a aci	taaa	caga	acce	caat	aaa	-22''	tcccac
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<212> PRT

agcc

<213> Homo Sapiens

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<211> 1087

<212> DNA

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780

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<211> 752

<212> PRT

<213> Homo Sapiens

<400> 579

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Cys 145	Ile	His	Cys	Ser		Gln	Gly	Phe	Glu		Pro	Asp	Asn	Lys	
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	Lys			165					170					175	
Ile	Arg	Cys	Glu 180	Phe	۷al	Lys	Phe	Gln 185	Asp	Arg	Trp	Glu	Val 190	Ile	Leu
Ala	Asp			Gly	Ile	Ile			Asp	Met	Ile	Ser		Tyr	Ala
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	Ser 210					215					220				
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Val	Ile	Asp			Glu	Tyr	Phe			Gln	Phe	Ala	_	255 Thr	Glu
7	T 011	43	260	T	~1	77-7	~ 1	265	~7	1			270		
	Leu	275					280					285			
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Ile	Val	Arg	Tyr	Arg	Glu	Asp	Gly	His	Tyr	Tyr	Arg	Ala	Leu	Ile	Thr
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Asn	Ile	Glu	Asp 340	Cys	Val	Asp	Pro	Lys 345	Ala	Leu	Trp	Ala	Ile 350	Pro	Ser
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Phe	Asn 370		Ser	Glu	Gly	Leu 375		Ser	Gln	Glu			Asp	Tyr	Phe
Tvr	Glu	Tle	Tle	Thr	Glu		Val	T.ean	Glu	Tla	380 Thr	T10	T 033	<i>م</i> ا	T] ^
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	Arg			405					410					415	
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Pro	Cys	Lys	500 Asp	Lys	Ile	Asp	Thr	505 Glu	Glu	Leu	Glu	Glv	510 Glu	Leu	Glu
		515					520					525			
	His 530					535					540				
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545	_	_	_	_	550		_			555					560
GLU	Leu	Asn	Ser	Leu 565	Glu	Val	Pro	Leu	Ser 570	Pro	Asp	Asp	Glu	Ser 575	Lys
Glu	Phe	Leu	Glu	Leu	Glu	Ser	Ile	Glu	Leu	Gln	Asn	Ser	Leu	Val	Val

580 585 590 Asp Glu Glu Lys Gly Glu Leu Ser Pro Val Pro Pro Asn Val Pro Leu 600 605 Ser Gln Glu Cys Val Thr Lys Gly Ala Met Glu Leu Phe Thr Leu Gln Leu Pro Leu Ser Cys Glu Ala Glu Lys Gln Pro Glu Leu Glu Leu Pro 630 635 Thr Ala Gln Leu Pro Leu Asp Asp Lys Met Asp Pro Leu Ser Leu Gly 645 650 Val Ser Gln Lys Ala Gln Glu Ser Met Cys Thr Glu Asp Met Arg Lys 660 665 Ser Ser Cys Val Glu Ser Phe Asp Asp Gln Arg Arg Met Ser Leu His 680 Leu His Gly Ala Asp Cys Asp Pro Lys Thr Gln Asn Glu Met Asn Ile 695 Cys Glu Glu Glu Phe Val Glu Tyr Lys Asn Arg Asp Ala Ile Ser Ala 710 715 Leu Met Pro Phe Ser Leu Arg Lys Lys Ala Val Met Glu Ala Ser Thr 725 730 Ile Met Val Tyr Gln Ile Ile Phe Gln Asn Tyr Arg Thr Pro Thr Leu 740 745 750

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<213> Homo Sapiens

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<211> 312

<212> PRT

<213> Homo Sapiens

<400> 581

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<400> 582

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<211> 872

<212> PRT

<213> Homo Sapiens

<400> 583

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	370					375					380			Asp	
385					390					395				Pro	400
				405					410					Pro 415	
			420	•				425	_			_	430	His	
		435					440					445		Thr	
	450					455					460			Pro	
Gly 465	Val	Pro	Tyr	Pro	Glu 470	Ala	Lys	Ile	Gly	Arg 475	Phe	Val	Val	Gln	Asn 480
Val	Ser	Ala	Gln	Lys 485	Asp	Gly	Glu	Lys	Ser 490	Arg	Val	Lys	Val	Lys 495	Val
			500					505					510	Met	
		515					520					525		Asp	
	530					535					540		_	Lys	
545					550					555				Gln	560
				565					570					Thr 575	
			580					5 85					590	Lys	
		595					600				_	605		Asn	
	610					615					620		_	Asp	
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			660					665					670	Ile	-
		675					680					685		Glu	_
	690					695					700			Val	_
705					710					715				Arg	720
				725					730					Gln 735	
			740					745					750	Asp	
Lys	Tyr	Asn 755	His	Ile	Asp	Glu	Ser 760	Glu	Met	Lys	Lys	Val 765	Glu	Lys	Ser

Val Asn Glu Val Met Glu Trp Met Asn Asn Val Met Asn Ala Gln Ala 775 Lys Lys Ser Leu Asp Gln Asp Pro Val Val Arg Ala Gln Glu Ile Lys 790 795 Thr Lys Ile Lys Glu Leu Asn Asn Thr Cys Glu Pro Val Val Thr Gln 810 Pro Lys Pro Lys Ile Glu Ser Pro Lys Leu Glu Arg Thr Pro Asn Gly 820 825 Pro Asn Ile Asp Lys Lys Glu Glu Asp Leu Glu Asp Lys Asn Asn Phe 840 845 Gly Ala Glu Pro Pro His Gln Asn Gly Glu Cys Tyr Pro Asn Glu Lys 860 Asn Ser Val Asn Met Asp Leu Asp 865 870

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<211> 687

<212> PRT

<213> Homo Sapiens

<400> 585

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Pro	Pro 290	Glu	Lys	Glu	Lys	Ser 295	Ser	Leu	Ala	Lys	Ala 300	Ala	Ser	Pro	Ile
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Lys	Val	Thr 355	Asn	Gly	Cys	Asn	Asn 360	Leu	Gly	Ile	Ile	Met 365	Asp	His	Ser
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	450					455				Val	460				-
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<211> 1898 <212> DNA <213> Homo Sapiens

<400> 586

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<400> 587

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Val Glu Lys Ser Glu Leu Ala Pro Thr Arg Gly Ala Val Met Glu Gln
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Gly Thr Ser Ser Met Thr Glu Ser Ser Pro Arg Ser Met Leu Gly
                    150
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Tyr Asp Arg Asp Gly Arg Gln Val Ala Ser Asp Ser His Val Val Pro
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                                    170
Ser Val Pro Gln Asp Val Pro Ala Phe Val Arg Pro Ala Arg Val Pro
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Thr Arg Asp Gly Gly Ala Gly Ser Ser Ala Pro Pro Pro Ser Asp Met
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                            200
Gly Val Gly Gln Ala Ser His Pro Gln Thr Leu Gly Arg Ala Leu
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Gly Ser Pro Arg Arg Pro Asp His Gln Asp Val Ser Ser Pro Ala Lys
                    230
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Thr Val Gly Arg Phe Ser Val Val Ser Thr Gln Asp Glu Trp Thr Leu
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Ala Ser Pro His Ser Leu Arg Tyr Ser Ala Pro Pro Asp Val Tyr Leu
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Asp Glu Ala Pro Ser Ser Pro Asp Val Lys Leu Ala Val Arg Arg Ala
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Gln Thr Ala Ser Ser Ile Glu Val Gly Val Gly Glu Pro Val Ser Ser
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Asp Ser Gly Asp Glu Gly Pro Arg Ala Arg Pro Pro Val Gln Lys Gln
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Ala Ser Leu Pro Val Ser Gly Ser Val Ala Gly Asp Phe Val Lys
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Ala Thr Ala Ser Cys Arg Gly Leu Leu Gly Pro Ala Ser Leu Gly Pro
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Glu Thr Pro Ser Arg Val Gly Met Lys Val Pro Thr Ile Ser Val Thr
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Ser Phe His Ser Gln Ser Ser Tyr Ile Ser Ser Asp Asn Asp Ser Glu
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<211> 707

<212> DNA

<213> Homo Sapiens

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600

660

666

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540

600

660

688

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aagagaagga ngacgangag aacacgtcag cggctganca ctcggaagaa ganaanaagg
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gagtgatatn tttccatttc tccgcttttt atagttaagg cattttttnc tnctctgaca
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tgtcanccca ngcaanaggg ccaanatgca attcagggat ccntgggaca ggtccaaaat
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gatntaatga gccaggggtt tcatcctgaa aqaqaccct ctqacctana aaaaqtqaaa
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gatttcagag ccacgccctt cccattctgc tctgcagggt ccttqctqct ctcccatttq
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tagaaggcat ceteggagat caceteeteg teatatagae aateaaaaa cateegeage
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cettetetgt atetgantet aggtaettga gtaagategg cactetetge ttgataacag
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cagtgtccac tctgaaggta naagaatcng gttattatag cttgctttaa caaacagcng
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agactgaaat ctttttctaa ataatgtata tacatgtttt gtgatctgta cacacttatt
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600

660

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780

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<212> PRT

<213> Homo Sapiens

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-395-

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agtccattgg caccgagaac accgaggaga accggcgctt ctaccgccag ctgctgctga
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420

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<211> 364

<212> PRT

<213> Homo Sapiens

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Gly Gly Gln Ser Glu Glu Glu Ala Ser Ile Asn Leu Asn Ala Ile Asn
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                                                 285
Lys Cys Pro Leu Leu Lys Pro Trp Ala Leu Thr Phe Ser Tyr Gly Arg
                        295
                                             300
Ala Leu Gln Ala Ser Ala Leu Lys Ala Trp Gly Gly Lys Lys Glu Asn
305
                    310
                                         315
Leu Lys Ala Ala Gln Glu Glu Tyr Val Lys Arg Ala Leu Ala Asn Ser
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<213> Homo Sapiens

<400> 801

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<212> PRT

<213> Homo Sapiens

<400> 802

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165
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Glu Thr Pro Pro Pro Pro Pro Pro Asn Glu Ile Ser Pro Pro His Ala
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Val Glu Glu Glu Asp Asp Asp Trp Gly Glu Asp Thr Thr Glu Glu
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Ala Gln Arg Arg Met Asp Glu Ile Ser Asp His Ala Lys Gly Leu
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Leu Phe Asp Phe Val Lys Lys Lys Glu Glu Gly Ile Ile Asp Ser
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Ser Asp Lys Asp Ile Val Ala Glu Ala Glu Arg Leu Asp Val Lys Ala
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Met Gly Pro Leu Val Leu Thr Glu Val Leu Phe Asp Glu Lys Ile Arg
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Glu Gln Ile Lys Lys Tyr Arg Arg His Phe Leu Arg Phe Cys His Asn
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Asn Lys Lys Ala Gln Arg Tyr Leu Leu His Gly Leu Glu Cys Val Val
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Ala Met His Gln Ala Gln Leu Ile Ser Lys Ile Pro His Ile Leu Lys
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Glu Met Tyr Asp Ala Asp Leu Leu Glu Glu Glu Val Ile Ile Ser Trp
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Ser Glu Lys Ala Ser Lys Lys Tyr Val Ser Lys Glu Leu Ala Lys Glu
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Ile Arg Val Lys Ala Glu Pro Phe Ile Lys Trp Leu Lys Glu Ala Glu
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Glu Glu Ser Ser Gly Gly Glu Glu Glu Asp Glu Asp Glu Asn Ile Glu
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      <210> 803
      <211> 2251
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<212> DNA

<213> Homo Sapiens

<400> 803

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<210> 804

<211> 609

<212> PRT

<213> Homo Sapiens

<400> 804

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Ala	Ser	Leu	Gln	Lys	Phe	Gly	Glu	Arg	Ala		Lys	Ala	Trp	Ala	Val
225					230					235					240
Ala	Arg	Leu	Ser	Gln 245	Arg	Phe	Pro	Lys	Ala 250	Glu	Phe	Ala	Glu	Val 255	Ser
Lys	Leu	Val	Thr 260	Asp	Leu	Thr	Lys	Val 265	His	Thr	Glu	Cys	Cys 270	His	Gly
Asp	Leu	Leu 275	Glu	Cys	Ala	Asp	Asp 280	Arg	Ala	Asp	Leu	Ala 285	Lys	Tyr	Ile
Cys	Glu 290	Asn	Gln	Asp	Ser	Ile 295	Ser	Ser	Lys	Leu	Lys 300	Glu	Cys	Cys	Glu
Lys 305	Pro	Leu	Leu	Glu	Lys 310	Ser	His	Cys	Ile	Ala 315	Glu	Val	Glu	Asn	Asp 320
Glu	Met	Pro	Ala	Asp 325	Leu	Pro	Ser	Leu	Ala 330	Ala	Asp	Phe	Val	Glu 335	Ser
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Met	Phe	Leu 355	Tyr	Glu	Tyr	Ala	Arg 360	Arg	His	Pro	Asp	Tyr 365	Ser	Val	Val
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Cys 385	Ala	Ala	Ala	Asp	Pro 390	His	Glu	Cys	Tyr	Ala 395	Lys	Val	Phe	Asp	Glu 400
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Glu	Leu	Phe	Lys 420	Gln	Leu	Gly	Glu	Tyr 425	Lys	Phe	Gln	Asn	Ala 430	Leu	Leu
Val	Arg	Tyr 435	Thr	Lys	Lys	Val	Pro 440	Gln	Val	Ser	Thr	Pro 445	Thr	Leu	Val
Glu	Val 450	Ser	Arg	Asn	Leu	Gly 455	Lys	Val	Gly	Ser	Lys 460	Cys	Cys	Lys	His
Pro 465	Glu	Ala	Lys	Arg	Met 470	Pro	Cys	Ala	Glu	Asp 475	Tyr	Leu	Ser	Val	Val 480
Leu	Asn	Gln	Leu	Cys 485	Val	Leu	His	Glu	Lys 490	Thr	Pro	Val	Ser	Asp 495	Arg
			500					505				_	510	Cys	
Ser	Ala	Leu 515		Val	Asp	Glu	Thr 520		Val	Pro	Lys	Glu 525	Phe	Asn	Ala
Glu	Thr 530	Phe	Thr	Phe	His	Ala 535	_	Ile	Cys	Thr	Leu 540		Glu	Lys	Glu
545					550					555			_		Lys 560
				565					570			_	_	Phe 575	
			580					585					590	_	Phe
Ala	Glu	Glu 595		Lys	Lys	Leu	Val 600		Ala	Ser	Gln	Ala 605		Leu	Gly
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<211> 1356 <212> DNA <213> Homo Sapiens

<400> 805

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<210> 806

<211> 299

<212> PRT

<213> Homo Sapiens

<400> 806

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Asp His Lys Ile Phe Tyr Tyr Ile Asp Ser Leu Ser Tyr Ser Val Asp
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Ala Phe Asp Tyr Asp Leu Gln Thr Gly Gln Ile Ser Asn Arg Arg Ser
                                185
Val Tyr Lys Leu Glu Lys Glu Glu Gln Ile Pro Asp Gly Met Cys Ile
                            200
                                                 205
Asp Ala Glu Gly Lys Leu Trp Val Ala Cys Tyr Asn Gly Gly Arg Val
                        215
Ile Arg Leu Asp Pro Val Thr Gly Lys Arg Leu Gln Thr Val Lys Leu
                    230
Pro Val Asp Lys Thr Thr Ser Cys Cys Phe Gly Gly Lys Asn Tyr Ser
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Glu Met Tyr Val Thr Cys Ala Arg Asp Gly Met Asp Pro Glu Gly Leu
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Leu Arg Gln Pro Glu Ala Gly Gly Ile Phe Lys Ile Thr Gly Leu Gly
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<210> 807

<211> 1980

<212> DNA

<213> Homo Sapiens

<400> 807

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<210> 808

<211> 659

<212> PRT

<213> Homo Sapiens

<400> 808

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340 345 350 Leu Leu Val Ala Lys Glu Lys Gln His Glu Glu Ser Leu Arg Thr Ile

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Leu Gly Leu Glu Cys Glu Arg Ile Lys Glu Asp Ser Asp Glu Gln Ile
Lys Gln Leu Glu Asp Ala Leu Lys Asp Val Gln Lys Arg Met Tyr Glu
                    470
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Ser Glu Gly Lys Val Lys Gln Met Gln Thr His Phe Leu Ala Leu Lys
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Glu His Leu Thr Ser Glu Ala Ala Ile Gly Asn His Arg Leu Met Glu
            500
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Glu Leu Lys Asp Gln Leu Lys Asp Met Lys Ala Lys Tyr Glu Gly Ala
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Ser Ala Glu Val Gly Lys Leu Arg Asn Gln Ile Lys Gln Asn Glu Leu
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Leu Val Glu Gln Phe Arg Arg Asp Glu Gly Lys Leu Val Glu Glu Asn
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Lys Arg Leu Gln Lys Glu Leu Ser Met Cys Glu Thr Glu Arg Asp Lys
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Lys Gly Arg Arg Val Ala Glu Val Glu Gly Gln Val Lys Glu Leu Leu
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Ala Lys Leu Thr Leu Ser Val Pro Thr Glu Lys Phe Glu Ser Met Lys
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Ser Leu Leu Ser Ser Glu Val Asn Glu Lys Val Lys Lys Ile Gly Glu
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Thr Glu Arg Glu Tyr Glu Lys Ser Leu Thr Glu Ile Arg Gln Leu Arg
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<210> 809

<211> 1725

<212> DNA

<213> Homo Sapiens

<400> 809

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<210> 810

<211> 355

<212> PRT

<213> Homo Sapiens

<400> 810

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